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Reactions across stages of in vitro fertilization-embryo transfer (IVF-ET)

in subsequently Pregnant and Non-pregnant women using a daily

monitoring inventory

Jacky Boivin

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Abstract

Reactions across stages of in vitro fertilization-embryo transfer (IVF-ET)
in subsequently Pregnant and Non-pregnant women using a daily
monitoring inventory

Jacky Boivin, Ph.D.
Concordia University, 1995

IVF-ET is a multi-stage treatment which involves growth and
maturation of follicles through hormone administration, retrieval of oocytes
from the ovaries, artificial fertilization outside the womb and subsequent
implantation of embryos to the uterus. One concern associated with the use
of this intervention has been the emotional distress couples can experience
and its effect on chances of conception with treatment. To date, information
available on women's reactions during treatment has been based on
retrospective accounts which are potentially confounded by a number of
factors. The objectives of the present study were to examine 1) emotional,
physical and behavioral reactions experienced during IVF-ET, 2) the
relationship between psychological factors and the success or failure of this
treatment, and 3) factors that predict emotional distress during treatment. In
the first phase of the study, women were interviewed and completed a battery
of questionnaires which assessed marital satisfaction, anxiety, infertility-
specific distress and coping style. In the second phase, women monitored
their emotional, physical and behavioral reactions daily for one complete
IVF-ET cycle. Three days after the results of treatment were known, patients
completed an anxiety inventory and a short questionnaire that asked them to
recall the stress of the various stages of IVF-ET. Based on the outcome of
treatment women were assigned to the Non-pregnant (n=24) or Pregnant
group (n=18). Biological data on the progress of IVF-ET was collected from
medical charts after treatment. On average, women were in their mid-thirties,
had been infertile for 4.33 years (SD=2.06), and had received treatment for 2.58
years (SD=1.73). Overall, the Non-pregnant and Pregnant groups were
comparable in terms of their general psychological and interpersonal
functioning.

One major finding of the study was that the Non-pregnant group
experienced significantly more distress during treatment than the Pregnant

group ($F_{(8, 304)}=13.56$, $p < .001$). Higher distress in the Non-pregnant group was possibly due to the greater negative feedback women in this group received about the progress of their IVF-ET trial. Another important finding was that patients recalled the period during which they waited for the results of treatment as more stressful than their ongoing experience of it as reported on the daily monitoring inventory ($F_{(3, 114)}=39.58$, $p < .001$). A number of hypotheses were offered to account for the difference between retrospective and prospective ratings of treatment distress. Finally, it was found that several factors assessed prior to treatment could predict women at risk for greater distress during treatment. A number of methodological, conceptual and clinical issues were discussed in relation to the findings of the study.

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Reactions across stages of in vitro fertilization-embryo transfer (IVF-ET) in subsequently Pregnant and Non-Pregnant women using a daily monitoring inventory

The birth of Louise Brown in 1978, the first child conceived through in vitro fertilization-embryo transfer (IVF-ET), marked the beginning of a new era in technologies designed to help couples achieve a pregnancy. Since her birth, more than 10, 000 children have been conceived by this technique and several hundred IVF-ET centres have been established throughout the world (Mazure, Milki, Takefman & Lake-Polan, 1992). Recent statistics on the use of IVF-ET indicate that almost 25, 000 cycles were initiated in 1991 in the United States and Canada, an increase of 20% from the previous year (Society for Assisted Reproductive Techniques & American Fertility Society (SART & AFS), 1993). The widespread use of this medical intervention to achieve pregnancy has generated much debate and controversy in Canada (Royal Commission on New Reproductive Technologies, 1993), as well as in countries throughout the world (Office of Technology Assessment (OTA), 1988).

One persistent concern has been the emotional distress couples may experience over the course of this 45 day, multi-stage intervention and its effect on their chances of conception with treatment. IVF-ET can be a physically and emotionally demanding treatment both because of the medical procedures involved and because it usually represents the couple's final hope for a pregnancy (Dennerstein & Morse, 1988). To date, most of the studies carried out with IVF-ET patients have focused on either the psychological profile of women about to begin treatment or on the impact of treatment failure on women's psychological functioning (Dennerstein & Morse, 1988; Mazure & Greenfeld, 1989; Mazure, Takefman, Milki, Lake-Polan, 1992).

Consequently, little information is available on women's reactions during IVF-ET.

The objectives of the present study were to examine 1) the emotional, physical and behavioral reactions women experience during treatment, 2) the relationship between emotional reactions and IVF-ET outcome and 3) the factors that may predict emotional distress during the various stages of IVF-ET. In order to achieve these objectives, subjects in this study were interviewed and completed a battery of psychological questionnaires prior to treatment and then monitored their reactions daily using a self-report, multi-item inventory for one complete IVF-ET cycle. Based on whether pregnancy was achieved, women were assigned to the Non-pregnant or Pregnant group and their treatment reactions compared. Baseline psychological variables assessed prior to treatment were used to predict emotional distress at each stage of the IVF-ET process. Before reviewing the psychological studies on IVF-ET, a description of the medical and social aspects of IVF-ET will be presented.

I. Medical and social aspects of IVF-ET participation

The precise medical regimen used in IVF-ET differs depending on the clinic at which it is performed. The following description is based on the regimen used with subjects in this study. IVF-ET depends on the controlled use of various synthetic hormones to artificially re-create the menstrual cycle. The first step in the process is to prevent the naturally occurring hormonal changes of the menstrual cycle. In the natural menstrual cycle, the hypothalamus synthesizes gonadotrophin releasing factor (GnRH) which is responsible for the release of pituitary hormones and the massive surge in leutenizing hormone that triggers ovulation (Yen, 1986). By administering a

GnRH analog (GnRH-a) at the start of IVF-ET the natural effect of GnRH on pituitary hormones is blocked as is the spontaneous occurrence of ovulation. This hormone analog is self-administered by patients intramuscularly for 15 days prior to the administration of human menopausal gonadotrophin (hMG). In the second stage of IVF-ET, the growth and maturation of ovarian follicles containing oocytes are initiated with the use of hMG. The hormone is administered by a nurse for a period of 9-12 days, in conjunction with the self-administered GnRH-a. Because the response to hMG is unique to each woman, it is necessary to carry out daily blood tests, starting on the fifth day of administration, to calibrate the dosage of hMG. Ultrasounds are also used to monitor the maturing follicles and to pinpoint the optimal time for oocyte retrieval.

The next stages in the IVF-ET process are ovulation induction, oocyte retrieval and embryo transfer. When the follicles are large and mature enough, women receive an injection of human chorionic gonadotrophin (hCG) to conclude oocyte maturation prior to retrieval. Thirty-six hours after hCG the oocytes are removed by ultrasound-guided aspiration of the fluid inside the follicles. A local anesthetic is used during the retrieval because the aspiration needle pierces the vaginal wall to reach the ovaries. Once the oocytes have been collected they are placed with the husband's sperm in a culture dish. The husband must be able to provide fresh sperm within two hours of the retrieval. Couples must then wait 48 hours to find out whether viable embryos have been created. During this 48 hour period, fertilization and cleavage occur. Once the embryos have developed to at least the two-cell stage, a maximum of three embryos are placed into the uterus using a catheter. The next stage in the IVF-ET process is the two week waiting period that follows the transfer, after which couples find out whether IVF-ET has

been successful. Progesterone suppositories are used from the day of embryo transfer until the 12th week of pregnancy. Progesterone facilitates implantation and potentially reduces the risk of miscarriage by enhancing uterine receptivity to the embryo.

The final stage of IVF-ET is the pregnancy test scheduled 14 days after the transfer, which, if positive, indicates that a biochemical pregnancy has been achieved. A biochemical pregnancy is established when hCG blood levels are above 25 i.u./L. If this test is positive, an ultrasound is scheduled for two weeks later to visualize the gestational sac and fetal heartbeat, the presence of which establishes a clinical pregnancy. Recent statistics based on IVF-ET trials completed in 1991 indicate that 85.5% of women will reach the stage of oocyte retrieval and of these 87.1% will go on to successful embryo transfer (SART & AFS, 1993). Approximately, 16% of couples who initiate an IVF-ET cycle will achieve a clinical pregnancy and 13% a live birth (SART & AFS, 1993). In summary, the six basic stages of IVF-ET are: 1) prevention of naturally occurring menstrual cycle changes (hormonal suppression), 2) growth and maturation of oocytes (ovarian stimulation), 3) ovulation induction, 4) oocyte retrieval and embryo transfer, 5) two week waiting period and, 6) pregnancy test. The entire IVF-ET cycle requires approximately 45 days.

It is clear from this description that IVF-ET can be stressful for a variety of reasons. First, the chances of success with this intervention are relatively low. For many couples IVF-ET represents their final hope for a pregnancy because most choose or are accepted for this intervention only after other medical alternatives have failed (Collins, Freeman, Boxer & Tureck, 1992; Hearn, Yuzpe, Brown & Casper, 1987). Several studies have shown that women tend to overestimate their chances of success at the start of IVF-ET relative to information provided by medical staff (Collins et al., 1992;

Haseltine et al., 1985; Leiblum, Kemmann & Lane, 1987). Thus their high hopes for a pregnancy are held in the context of a relatively new technology where the chances of success are still low, that is, where the majority of trials fail.

Second, the physical effects associated with IVF-ET can be burdensome. The Compendium of Pharmaceutical Specialities (Canadian Pharmaceutical Association (CPA), 1994) lists a number of potential side-effects for GnRH-a, hMG, hCG and the various anesthetics used during oocyte retrieval. The most frequent of these include: hot flashes/sweats, headaches, breast tenderness, ovarian pain, abdominal discomfort, dizziness, local reactions at injection site and mood fluctuations. Because the side-effects of these medications differ, it can be expected that women will experience a range of symptoms depending on the stage of IVF-ET they are currently involved in. Indeed, one study found that ovarian stimulation (hMG administration) was associated with fatigue, weight gain and headaches, whereas oocyte retrieval was associated with breast tenderness, abdominal cramps and nausea (Leiblum et al., 1987).

Third, the time commitment and practical demands can be disrupting. During the initial stages of IVF-ET women must attend the clinic on a daily basis to receive injections, take blood tests and undergo ultrasounds and surgical procedures for oocyte retrieval and embryo transfer. These practical demands may disrupt daily activities at work and/or interfere with their social life. Treatment may also affect the marital relationship. Because couples tend to be reluctant to discuss their infertility with others (Menning, 1980), spouses are usually each others principal source of support during IVF-ET (Callan & Hennessey, 1988). Although infertile couples have generally been shown to have a strong marital relationship (Mazure, Takefman, Milki,

Lake-Polan, 1992), the emotional and physical demands of IVF-ET, coupled with limited sources of social support, may place an unusual burden on their relationship.

Finally, IVF-ET is one of the most costly infertility treatments available. A single trial of this intervention costs between $4,500 and $7,000 dollars in Québec depending on the specific medical regimen used. Because national healthcare does not cover IVF-ET and since most patients do not have medical insurance for the substantial costs of medication, most couples must assume all the financial costs of IVF-ET (P. Miron, personal communication, January 10, 1994).

In summary, it is reasonable to hypothesize that IVF-ET can be stressful to patients for a variety of reasons. The treatment cycle is protracted, the physical procedures invasive and the hormonal supplements can cause side effects. In addition, the couple must contend with the considerable financial costs of the procedures, the time commitment required and the potential disruptions to their relationship, social and work life. Finally, for many couples IVF-ET represents a "last resort" to become biological parents, and this hope is held in the context of an intervention with a relatively low success rate.

II. Emotional aspects of IVF-ET

Although there has been discussion in the literature about the stress of IVF-ET and its potential impact on outcome (Dennerstein & Morse, 1988; Mazure & Greenfeld, 1989; Seibel & Levin, 1987), no study has documented women's reactions during the IVF-ET cycle. As mentioned previously, most of the IVF-ET studies to date have focused on either the psychological profile of couples about to begin a treatment cycle or on women's reactions to IVF-ET

failure (Dennerstein & Morse, 1988; Mazure & Greenfeld, 1989; Mazure, Takefman, Milki, Lake-Polan, 1992). It is only from the latter studies that information about emotional reactions during treatment can be extrapolated. These findings will be presented next, followed by a discussion of methodological issues.

In terms of the overall impact of IVF-ET, women who have undergone at least one cycle, typically rate it as stressful. Leiblum and coworkers (Leiblum et al., 1987) found that 35% of women rated it as very stressful, whereas 22% of women found it to be minimally stressful. Higher ratings of stress have been reported in other studies. Mahlstedt et al. (Mahlstedt, MacDuff & Bernstein, 1987) and Freeman et al. (Freeman, Rickels, Tausig, Boxer, Mastroianni, & Tureck, 1987) reported that approximately 80% of their samples reported IVF-ET to be stressful or extremely stressful. Connolly and colleagues (Connolly, Edelmann, Bartlett, Cooke, Lenton, & Pike, 1993) reported that on average the overall stress of treatment was rated as moderate to extremely stressful.

As mentioned previously, there are usually six stages to the IVF-ET procedure: hormonal suppression, ovarian stimulation, ovulation induction, oocyte retrieval, embryo transfer, two week waiting period and pregnancy test. Rankings of the stress of the various stages are fairly consistent. The two week waiting period and finding out that IVF-ET was not successful have been ranked as most stressful (Baram, Tourtelot, Muechler & Huang, 1988; Callan & Hennessey 1988; Connolly et al., 1993; Leiblum et al., 1987). Other stressful time points include waiting to find out whether oocytes have been retrieved (Callan & Hennessey, 1988; Connolly et al., 1993) and whether oocytes have been fertilized (Connolly et al., 1993). These findings suggest that what women recall as having been most stressful or anxiety-provoking during IVF-

ET were not the medical procedures per se, but rather the period during which they waited for results at the various stages of the process.

Because the studies from which the previous findings were extrapolated were not designed specifically to examine distress experienced during treatment, the findings are limited for a number of reasons. First, all data were obtained through retrospective reports in women for whom IVF-ET was unsuccessful. In studies that compare psychological functioning prior to and after IVF-ET, it has been found that unsuccessful treatment is associated with acute periods of depression (Litt, Tennen, Affleck, & Klock, 1992), elevated anxiety (Newton, Hearn, Yuzpe, 1990), anger and frustration (Leiblum et al., 1987) and a variety of other reactions, including suicidal thoughts (Baram et al., 1988). Perceptions of treatment stress may be expected to be influenced by these emotional reactions to treatment failure. Indeed, studies examining the impact of emotional state on recall have generally found that negative emotional states lead to more negative perceptions of previous life events, whereas positive states have the reverse effect (Williams, 1992). In support of this, one study found that women who did not get pregnant with IVF-ET were more depressed than their pregnant counterpart and recalled their "emotional experience" (term not defined) during IVF-ET as more negative (Freeman et al., 1987).

The accuracy of recall of treatment stress in some of these studies may also be biased by distortions in memory that accompany the passage of time. In the design of some of these studies, recall is requested a few weeks after treatment (Leiblum et al., 1987; Mahlstedt et al., 1987; Connolly et al., 1993) whereas in others more than a year (Freeman et al., 1987) or several years (Baram et al., 1988) after treatment. It has been found that individuals reconceptualize their emotional experiences of an event once the event has

been concluded (Conway & Ross, 1984; Ross, 1989; Thomas & Diener, 1990). Alterations can be made on the basis of new experiences, changing attitudes, and/or beliefs. When recall is requested many weeks or months after treatment there is greater opportunity for this sort of revision to take place, making retrospective accounts difficult to interpret.

A final limitation of these retrospective studies is the measurement of emotional reactions. As mentioned, it usually has consisted of an overall rating based on a single Likert item of the stress dimension (i.e., "not stressful" to "extremely stressful") which women use to rate the stress of the entire 45 day cycle. This type of global assessment is not very precise or descriptive of women's emotional experience during IVF-ET. As mentioned previously, women rate IVF-ET overall as moderately to extremely stressful. However, the various stages are not ranked as equally stressful suggesting that overall ratings obscure the fluctuating nature of stress over the course of treatment.

In summary, it would seem that distress fluctuates over the course of treatment, peaking when women wait for the results of treatment and discover that it was unsuccessful. However, these conclusions are based on retrospective reports that are potentially confounded by a number of factors. Given the stage-like nature of IVF-ET and the difficulties of using retrospective reports, greater understanding of emotional reactions during treatment would be gained from using a prospective methodology that uses multiple measurement points.

III. Neuroendocrinological impact of distress during IVF-ET

The link between emotional reactions, reproductive physiology and outcome in women undergoing infertility treatment is not clear. A number

of studies have provided evidence suggesting that psychological factors play a role in the outcome of donor insemination (DI). Earlier studies (Foldes, 1974; Glezerman, 1981) suggest that psychological factors may interfere with conception in DI by delaying or preventing ovulation, whereas others suggest a possible link between anxiety and implantation (Demyttenaere, Nijs, Steeno, Koninckx & Evers-Kiebooms, 1988; Schover, Greenhalgh, Richards & Collins, 1994). However, because follicular maturation and oocyte retrieval are medically controlled in IVF-ET, it has generally been assumed that these controls would override the negative effects of emotional reactions on IVF-ET outcome (Mazure, Takefman, Milki, Lake-Polan, 1992).

Only one study has examined the neuroendocrine impact of the anxiety women experience during oocyte retrieval (ORT) and embryo transfer (ET) in IVF-ET. Demyttenaere and colleagues (Demyttenaere, Nijs, Evers-Kiebooms & Koninckx, 1991) examined anxiety level, prolactin (PRL) and cortisol during these two stages of IVF-ET. These hormones were examined because it is well established that cortisol increases in response to stress (Grossman, 1991) and that PRL also increases in response to stress during gynaecological procedures (Koninckx, 1978; Harper, Lenton, & Cooke, 1985). Moreover, PRL is important to reproduction in that hyperprolactinemia is a cause of infertility that can be reversed with the administration of dopamine agonists that restore PRL to normal levels (Pepperell, 1981).

The results showed a significant increase in anxiety scores immediately prior to ORT as compared to pre-treatment levels, with anxiety returning to pre-treatment levels shortly after the procedure (Demyttenaere et al., 1991). A similar pattern was obtained with regard to ET, though anxiety levels were lower than those observed during ORT. Prolactin levels showed an anticipatory increase prior to ORT (as compared to pre-treatment levels) with

a significant rise during ORT. In contrast, PRL levels remained constant throughout ET. Although an anticipatory increase in cortisol was observed prior to ORT and ET, levels of these hormones began to decrease at the start of the procedures, returning to pre-treatment levels within the sampling period.

This study is important because it is the only one to document the neuroendocrine impact of women's subjective anxiety during IVF-ET. Although the increase in PRL during oocyte retrieval can be attributed to the physical stress of IVF-ET (i.e., medical procedures, anesthetic) (Lehtinen, Laatikainen, Koskimies & Hovorka, 1987), increases in PRL and cortisol prior to the retrieval and transfer are more likely attributable to anticipatory anxiety as indicated by subjective reports. Although PRL provides a potential mechanism through which subjective anxiety could affect outcome in IVF-ET, such transient rises in PRL have generally not been linked to lower pregnancy rates (Benker, Jaspers, Hausler, & Reinwein, 1990; Gonen & Casper, 1989).

In contrast, one recent study found a possible link between cortisol and implantation in IVF-ET (Michael et al., 1993). In this study, 11-beta-hydroxysteroid dehydrogenase (11beta-HSD) activity in cultured granulosa cells recovered from patients undergoing IVF-ET was assessed. Granulosa cells are found in the follicular fluid that surrounds the oocytes contained in the ovarian follicle. The presence of 11beta-HSD provides circumstantial evidence of cortisol since this enzyme inactivates cortisol by conversion to cortisone. Of the 32 patients whose cells had detectable levels of 11beta-HSD activity, 7 had fertilization failure (no oocytes fertilized) and none of the remaining patients became pregnant. In contrast, of the 32 patients showing no 11beta-HSD activity, 3 had fertilization failure and 75.9% (22) became pregnant (biochemical pregnancy). Since differences were not obtained for

the two groups on oocyte fertilisation, one possible interpretation for these findings is that oocyte exposure to cortisol, as measured by 11beta-HSD activity, had a negative impact on embryonic quality which, in turn, reduced the success of implantation.

Although the findings of Demyttenaere et al. (1991) and Michael et al. (1993) suggest a possible way in which psychological factors could impact on IVF-ET, firm conclusions about a possible relationship between these variables cannot be made until more studies examining this issue have been carried out.

IV. <u>Predictors of emotional reactions during IVF-ET</u>

A number of prospective studies have examined the predictors of poor adjustment to treatment failure in women undergoing IVF-ET. The major findings of these studies will be reviewed in the following section because the variables that predict poor adjustment to failure may als be related to women's experiences during treatment.

As mentioned previously, a number of studies have found that treatment failure is accompanied by an acute period of depression or anxiety-related symptoms. Given the emotional, physical and financial investments women make when undergoing IVF-ET, the emergence of symptoms of sadness, anger and frustration represents a normal reaction. However, a proportion of women will experience more severe and lasting reactions to treatment failure. Litt et al. (1992) found that 17% of women in their sample met DSM-III-R criteria (Diagnostic and Statistical Manual for Mental Disorders - Revised) for depressive adjustment disorder after treatment failure. Newton et al. (1990) found that after treatment failure, 25% of women reported mild to moderate levels of depression. In one retrospective study, it

was found that for a percentage of women (23%), feelings of distress persisted for more than a year after treatment failure (Baram et al., 1988).

Predictive analyses have shown that a number of factors can identify those at risk for poor adjustment to treatment failure. The single most important factor appears to be emotional functioning prior to treatment. Most studies show that women about to begin IVF-ET are not more likely to experience greater anxiety, depression, psychiatric symptomatology, marital dissatisfaction or sexual dysfunction on standardized measures than other infertile or fertile couples (Mazure, Takefman, Milki, Lake-Polan, 1992). However, those who score relatively lower within the normative range on these measures, particularly anxiety and depression, are more likely to experience greater distress when IVF-ET fails.

Another important factor is whether women have children. Leiblum et al. (1987) found that childless women experienced significantly more feelings of anger, emptiness and depression when IVF-ET failed than women with children. Newton et al. (1990) found that 15% of childless women were experiencing high levels of anxiety after IVF-ET (two standard deviations above norms) relative to women with children. Childlessness may be a critical factor because women without children have been shown to place greater emphasis on childbearing as a major life goal (Collins et al., 1992). Moreover, this factor has been shown to be related to infertility adjustment, in that women who have a more intense desire for children have more difficulty adjusting to or accepting their infertility (Abbey, Halman & Andrews, 1992; McEwan, Costello & Taylor, 1987). The findings with regard to childlessness are particularly important in light of the fact that the majority of IVF-ET patients do not have children (Mazure, Takefman, Milki & Lake-Polan, 1992).

A number of coping factors have also been examined in relation to adjustment to treatment failure. These factors are relevant to IVF-ET in that patients must cope with an intervention that is negative and whose outcome (success or failure) is unpredictable and beyond their control. Although many classes of coping strategies exist, these can be grouped into two broad categories: problem-focused and emotion-focused strategies (Lazarus & Folkman, 1984). While neither group of strategies is inherently more or less efficient, situational characteristics often determine which will be most beneficial in helping the individual maintain distress at an acceptable level. Problem-focused coping strategies are usually most useful in situations that permit some control in that these are aimed at changing or eliminating the threatening event. In contrast, emotion-focused coping is typically most useful when nothing can be done to alter a stressful situation, since these are aimed at managing the distress rather than the situation.

Better adjustment to IVF-ET failure appears to be related to a more positive outlook on the infertility problem, a greater sense of control over it (Litt et al., 1992) and the use of problem-focused coping strategies (Hynes, Callan, Terry & Gallois, 1992). In contrast, helplessness and avoidant (emotion-focused) strategies with regard to the infertility problem are related to poorer adjustment (Litt et al., 1992; Hynes et al., 1992). Although these findings appear counterintuitive because IVF-ET failure cannot be changed, they may not be. Though nothing can be done to change the fact that IVF-ET has failed, the couple still has many things to consider in terms of resolving the long-term problem of infertility. For instance, once treatment has failed couples must consider whether to terminate or continue with medical treatments or consider alternatives to IVF-ET (adoption, childlessness). In this context, avoidant coping strategies may be less beneficial because they may

interfere with women's ability to address these questions and therefore find an appropriate long-term solution.

While emotion-focused coping may not be effective in reducing distress when IVF-ET fails there is some evidence that such strategies may be beneficial during treatment. Callan and Hennessey (1988) asked 75 women to list the coping strategies they had used while undergoing IVF-ET (interval of time since attempt not reported). The principle ways in which women coped were by keeping a positive attitude about outcome and by using a variety of other strategies to keep their mind off treatment (e.g., keeping busy, reducing anxiety through relaxation techniques, being involved in other activities). Given the stage-like nature of IVF-ET, one might expect that emotion-focused coping might be more beneficial during the last two weeks of treatment when participation is minimal and patients wait for the results of treatment. In contrast, problem-focused strategies would be expected to be more beneficial during the initial stages of IVF-ET when patients are actively involved in the various medical procedures and in daily contact with medical staff and other patients. Unfortunately, in the Callan and Hennessey (1988) study patients were not asked to specify whether they had used different coping strategies over the course of treatment.

In summary, predictive studies in IVF-ET suggest a number of factors that may be related to distress when IVF-ET fails and this raises the possibility that these same factors may also be related to distress during treatment. These include pre-treatment anxiety or depression, childlessness and coping variables. Given the stage-like nature of treatment, one might expect that patients will use a variety of coping strategies during treatment.

The present study

The present study was designed to expand existing knowledge of women's reactions during IVF-ET and address methodological limitations in previous studies. First, the study was prospective. Subjects in this study monitored daily their reactions to treatment for one complete IVF-ET cycle, beginning with the first day of GnRH-a administration until the third day after the biochemical pregnancy test (approximately 45 days). This format was used to overcome the confounds associated with retrospective reports and to capture the potential fluctuations in reactions over the course of treatment. In addition, after treatment outcome was known, women completed a retrospective measure of treatment stress. Thus it was possible to examine the impact of the success or failure of IVF-ET on recall of emotional reactions during treatment.

Second, the reactions of both those who became pregnant with IVF-ET and those who did not were examined. Based on the outcome of IVF-ET, women were assigned to the Non-Pregnant or Pregnant group. Using this two group design it was possible to examine whether reactions during treatment were related to the outcome of IVF-ET.

The daily monitoring form used covered emotional, physical and behavioral reactions. The form lists a number of negative affective reactions (e.g., nervousness, frustration and sadness), potential side-effects (e.g., breast tenderness and ovarian pain), and items reflecting areas that may be affected by participation in IVF-ET (marital relationship, work and social life). In addition, a number of variables that could potentially be useful predictors of emotional reactions during treatment were assessed prior to IVF-ET. These included demographic and medical variables (e.g., number of children and years infertile), psychological variables (e.g., trait anxiety and coping style) and

infertility-specific measures of distress. It was thus possible to relate pre-treatment variables to emotional reactions during treatment.

Method

<u>Subjects</u>

Subjects consisted of 42 women who were about to begin a trial of IVF-ET at a private infertility clinic in Québec. While patients were not paid for their participation in the study, the $75.00 fee for the mandatory psychological evaluation prior to IVF-ET was waived. The selection criteria for the study were that women: 1) were accepted into the IVF-ET program; 2) had never attempted IVF-ET or a related reproductive technique (e.g., gamete intrafallopian transfer (GIFT); 3) underwent one complete IVF-ET cycle; 4) spoke and understood English or French sufficiently to be interviewed and to complete study materials in either language.

Over a 19 month period, from September, 1992 through April, 1994, a total of 72 women were referred to the study by their physician. Of these, 58.3% (42) completed the study. Table 1 shows the percentage of women (n=30) who were referred to the study and interviewed but who did not meet inclusion criteria or who withdrew. The principle reasons for exclusion were because the IVF-ET cycle was cancelled[1], or women's decision to withdraw from IVF-ET or the study[2]. The principle reason given for withdrawal from the study was time constraints.

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[1] The reasons for a cancelled protocol were: poor ovarian response to hMG (n=5); oocytes not retrieved or fertilized (n=3).

[2] Mean scores for demographic and psychological variables for women who withdrew from the study were not markedly different from those who continued in the study.

Table 1

<u>Percentage of subjects who were not followed beyond the initial interview</u>

Reasons	%
IVF-ET medical protocol cancelled	17.4
Withdrew from IVF-ET	15.2
Withdrew from study	13.0
Not accepted into IVF-ET	6.5
Pregnant on waiting list	6.5
Language difficulty	4.3
Hyperstimulation	2.2

Table 2 presents selected demographic variables for the 42 women who completed the study. Of these 42.8% (18) became pregnant with IVF-ET while the remaining 57.1% (24) did not achieve a biochemical pregnancy. The women were in their mid-thirties and had been married for seven to eight years. Although the Pregnancy group had significantly more years of education, a chi-square on occupation ($\underline{X}^2(4)=1.32$, $\underline{p} \geq .10$) revealed that women in both groups were principally employed in secretarial or managerial positions. The number of French and English-speaking subjects was also comparable in the two groups ($X^2(1)=.62$, $\underline{p} > .05$).

In terms of their medical history, the Non-pregnant and Pregnant group did not differ on years of infertility ($\underline{t}(40)=1.22$, $\underline{p} > .10$) or on number of years of other treatments for infertility ($\underline{t}(40)=.09$, $\underline{p} > .10$). On average, women had been infertile for 4.33 years ($\underline{SD}=2.06$) and had received treatment for 2.58 years ($\underline{SD}=1.73$). Table 3 presents selected medical characteristics of the sample. Approximately half of the women had no known previous conception (primary infertility). There were more women with unexplained infertility in the Pregnant group, while there were more women with tubal pathology in the Non-pregnant group (differences did not reach statistical significance). Women had tried a variety of treatments or interventions to resolve their infertility. Approximately half the women had tried medication (e.g., ovulation induction agents), and slightly fewer had tried artificial insemination (AI) with husband sperm. Consistent with the higher rate of tubal pathology in the Non-pregnant group, more women had surgery in this group than in the Pregnant group, although the difference was not significant. The demographic and medical profile of this sample was comparable to that reported for women initiating IVF-ET at other fertility clinics (Mazure, Takefman, Milki, & Lake-Polan, 1992).

Table 2

Means (SD) for selected demographic characteristics of the sample

	Group		
	Not Pregnant (n=24)	Pregnant (n=18)	t(40)
Age	33.54 (4.2)	33.00 (2.8)	.47
Years living together	6.75 (4.1)	8.17 (2.9)	1.26
Years education	12.29 (2.0)	14.39 (2.5)	2.09*

* p < .05

Table 3

Percentages (n) for selected medical characteristics of the sample

	Group		
	Not Pregnant (n=24)	Pregnant (n=18)	X^2
Primary infertility	66.7 (16)	50.0 (09)	$X^2(1)=1.19$
Diagnosis			
Unexplained (normal)	4.2 (01)	27.8 (05)	
Endocrine	12.5 (03)	16.7 (03)	
Tubal	62.5 (15)	38.9 (07)	
Male factor	12.5 (03)	5.6 (01)	
Male and female factor	8.3 (02)	11.1 (02)	$X^2(5)=5.83$
Treatments tried			
Medication	50.0 (12)	55.6 (10)	$X^2(1)=.13$
Surgery	58.3 (14)	38.9 (07)	$X^2(1)=1.56$
Insemination	33.3 (08)	38.9 (07)	$X^2(1)=.14$

Note. None of the chi-square values were significant.

Materials

There were two phases to the study. In the first phase, women were interviewed and completed a battery of questionnaires. In the second, women monitored their emotional, physical and behavioral reactions daily for one complete IVF-ET cycle using the Daily Record Keeping sheet (DRK). At the end of the IVF-ET cycle, women completed the Spielberger State-Anxiety Inventory (STAI-state) (Spielberger, Gorsuch, & Luschene, 1970) and a short questionnaire that asked them to recall their reactions during treatment.

Phase I:

Both the Interview and the questionnaires were available in English and French (materials not available in French were translated by a qualified translator for the study) (see Appendix A for material used during Phase I).

1. Interview: This structured interview was designed and used in a previous study on infertility treatment (i.e., superovulation) (Takefman, Boivin, & Brender, 1992) and was re-worded for use with IVF-ET patients. The interviews were conducted as part of patient screening prior to IVF-ET. From these interviews, the following data were collected for this study: (1) demographic (e.g., age and education) and detailed medical and gynecological information (e.g., years infertile and type of previous treatments); (2) women's reactions to the couple's infertility; and (3) information concerning the women's preparation for in vitro fertilization and expectations with regard to its success. Women responded to most items using five-point Likert scales. On average, the interviews took approximately one hour to complete and all interviews were carried out by the author.

At the end of the interview women were provided with a battery of five questionnaires to be completed at home during the week that followed the interview. The battery took approximately 30 minutes to complete and consisted of the following questionnaires:

1. Marital Adjustment Scale (MAS) (Kimmel & Van der Veen, 1974).

This version of the Locke-Wallace Marital Adjustment Scale (1959) was used to evaluate marital compatibility and satisfaction. It contains 23 items with scores weighted to reflect current sex differences in patterns of responding. This test is a highly reliable and well validated measure of marital adjustment (Schiavi, Derogatis, Kuriansky, O'Connor & Sharpe, 1979). The normative score for maritally-satisfied women is 100 (SD=16) (Nowinski & LoPiccolo, 1979). The MAS was used in this study because it is the marital compatibility measure most frequently used in infertility studies (Mazure & Greenfeld, 1989).

2. State-Trait Anxiety Inventory (STAI) (Spielberger et al., 1970).

This questionnaire measures two anxiety constructs: trait anxiety and state anxiety. The Trait scale asks individuals to describe how they generally feel with respect to 20 statements. The State scale requires subjects to indicate how they feel about the same 20 statements presently. The normative scores for working adult females between the ages of 19-39 is 36.15 (SD=9.5) and 36.17 (SD=11) for the Trait and State scale, respectively (Spielberger, 1983).

Measures of internal consistency are .92 and .81 for the Trait and State scale, respectively (Spielberger, 1983). In the present study, the standardized Cronbach alpha was .90 for the Trait scale and .89 for the State scale.

3. <u>Miller behavioural Style Scale (MBSS)</u> (Miller, 1979)

The MBSS consists of four hypothetical, stress-evoking life events of an uncontrollable nature. Each is followed by eight statements which represent different ways of coping in this situation. Subjects mark all statements which might apply to them. The measure yields two scores: a monitoring score which indicates the extent to which individuals use information-seeking to manage stressful situations and a blunting score which indicates the extent to which individuals use distraction to avoid such information.

Internal consistency was reported to be .75 for the monitoring score and .73 for the blunting score (Miller, personal communication, 1987). This scale has demonstrated good discriminant and predictive validity in that it has been shown to predict preference for information versus distraction in response to various threatening laboratory and clinical situations, including those involving gynaecological procedures (Miller & Mangan, 1983). Although earlier studies combined the monitoring and blunting scores, more recent studies have shown that the two dimensions are best considered separately when examining anxiety (Miller, 1987; Miller, Brody & Summerton, 1988). Internal reliability coefficients for the present sample were .63 and .60 for the monitoring and blunting scores, respectively.

4. <u>Social Desirability Scale (SDS)</u> (Crowne & Marlowe, 1964)

This scale identifies individuals who describe themselves in favourable, socially desirable terms. Social desirability taps into two separate factors: <u>self-deceptive positivity</u> (an honest but overly positive self-presentation) and <u>impression management</u> (self-presentation tailored to an audience). The SDS loads equally well on these two dimensions (Paulhus, 1984). The 33 True or False items are summed to obtain a total score. Crowne

and Marlowe (1964) report average scores for a normative sample of undergraduates of 16.8 ($\underline{SD}$=5.5) and report internal reliability coefficients of .88 for the scale. For the sample in this study the Cronbach alpha was .72. The SDS was used in this study because previous studies have shown that infertile women about to begin IVF-ET may be motivated to respond in socially desirable ways to insure that they receive treatment (Mazure et al., 1988).

5. Infertility Questionnaire (IFQ) (Bernstein, Potts & Mattox, 1985).

This 21 item measure was designed to assess adjustment to infertility. The IFQ consists of questions related to three domains (i.e., self-esteem, blame/guilt and sexuality). Each item is rated on a 5-point Likert scale. Research has indicated that the IFQ is a reliable and valid measure of infertility-related distress. Bernstein et al. (1985) reported internal reliability coefficient of .88 and test-retest reliability of .92. In this study, the Cronbach coefficient for the total score was .81. Convergent validity for the IFQ total score has been demonstrated through its moderate correlation with a well-validated, multidimensional inventory of psychological distress (SCL-90) (Bernstein et al., 1985).

For the purposes of this study four items were added to the IFQ to assess the extent to which the desire to have a child was a major focus of a woman's life (Childbearing focus). These items were selected because their sum has been shown to be the single most important factor predicting perceived treatment stress in a sample of 200 women entering an IVF-ET program (Collins et al., 1992). In the present study, the Cronbach alpha for the four items was .83.

Phase II:

1. <u>Daily Record-Keeping form (DRK)</u> (Takefman et al., 1992)

The DRK (see Appendix B) was the instrument used to measure changes in emotional, physical and behavioral reactions during the IVF-ET cycle. The DRK is divided into three subscales. The first subscale (emotional distress) contains 11 negative affective reactions (e.g., nervous, infertility stress and pessimism), whereas the second subscale lists 14 physical symptoms (e.g., nausea, fatigue and breast tenderness). A box, divided into three equal portions, is presented beside each symptom. Women blacken the portion of the square that corresponds to the degree to which they experienced each symptom that day (i.e., "none" to "severe"). The third subscale lists 10 items that may be influenced by treatment: relationship items (e.g., affection and argument with partner), socializing with family, optimism and pregnancy related items (e.g., feeling pregnant, pregnancy dreams). For this subscale, women check off the items they experienced that day. Instructions for the DRK are provided on the reverse side of the sheet.

Each sheet of the DRK contains seven days of daily monitoring (i.e., seven columns). For each day, women filled out the day of the treatment, the date, whether they had sexual intercourse that day, and indicated to what extent they had experienced each of the symptoms that day. In addition, they indicated whether they had received a medical intervention that day (e.g., hMG, oocyte retrieval) based on a list of treatment codes provided on the sheet. Women were instructed to complete the form at the end of each day.

The average sum of the items of the emotional subscale was used to assess treatment distress. The subscale total has been used in previous research on emotional reactions during infertility treatment (i.e., superovulation) (Takefman et al., 1992). The psychometric properties of the

distress subscale were examined in tnat study and it was found that 1) Cronbach alpha for the subscale was .90; 2) the sum of the items correlated moderately with the STAI-state anxiety inventory (r=.68); 3) the subscale total fluctuated across the treatment cycle in a manner consistent with expected changes; 4) subjects reported that the scale was neither difficult nor stressful to complete. In the present study, the Cronbach alpha coefficient computed on the averaged items across the IVF-ET cycle was .89. In this study, subjects also reported that completing the DRK was neither difficult ($\underline{M}$=1.56, $\underline{SD}$=.77) or stressful ($\underline{M}$=1.56, $\underline{SD}$=.63).

Reliability scores for the items of the two other subscales (i.e., physical and behavioral) has not been reported by the authors. However, the sum of the physical symptoms was found to fluctuate across a superovulation cycle according to expected changes (Takefman et al., 1992). Because the side effects associated with the medication used in IVF-ET differ, individual items, rather than a total physical score, will be analyzed in this study. The only exceptions were the items breast tenderness, ovarian pain, abdominal discomfort and abdominal bloating. Because these items all measure the physical effects of the estrogen rise induced by hMG administration (CPA, 1994) they were highly correlated in this sample (correlations ranging from .56 to .76). The sum of these items will be referred to as estrogen-related scores.

Similarly, the items of the behavioral subscale were also analyzed separately because these did not vary in the same way across the IVF-ET cycle. The items Sexual fantasy and Sexual desire were not analyzed. The validity of scores on these two items was questionable because women mentioned being reluctant to complete these at the time of the pre-interview. Thus, only 8 of the 10 items of the behavioral subscale were analyzed.

2. Retrospective Questionnaire:

This questionnaire (see Appendix B) was designed to be comparable to those commonly used in IVF-ET studies (c.f., Baram et al., 1988; Connolly et al., 1993; Leiblum et al., 1987). Women were asked to rate on 5-point Likert scales (i.e., "not stressful" to "extremely stressful") their response to: hMG administration, oocyte retrieval-embryo transfer, two week waiting period, and the pregnancy test. These retrospective ratings were compared to the prospective data obtained with the distress subscale of the DRK.

3. Medical Information:

At the end of the IVF-ET cycle, subjects' medical charts were examined and information about the medical aspects of IVF-ET, as recorded by the attending physicians, was obtained. The information collected assessed the quality of ovarian stimulation (e.g., blood estradiol levels per maturing follicle), oocyte retrieval (e.g., number of oocytes), fertilization (e.g., embryos created or transferred), and quality of sperm sample obtained for fertilization (e.g., motility). Pregnancy rates are generally higher in patients who have a better ovarian response to hMG (Hughes, King, Wood, 1989), have more mature oocytes (Hill et al., 1989), more embryos transferred (French in Vitro National Registry, 1993) and better sperm quality (Guzick, Balmaceda, Ord, Asch, 1989).

<u>Procedure</u>

Prior to soliciting the participation of infertility specialists at the infertility clinic, a proposal describing the study was approved by the Ethics Committees of Concordia University and the IVF-ET clinic. Infertility specialists and the nurse-coordinator at this clinic were briefed about the objectives of the study and encouraged to assist by discussing the project with patients initiating a first IVF-ET trial. Staff were asked to inform women that a research project conducted jointly by Concordia University and the clinic was being carried out and that the project would involve monitoring psychological and physical reactions on a daily basis. Patients were also informed by staff that though the psychological consultation was a requirement for admission, medical treatment was <u>not</u> contingent upon participation in the study.

Women who were interested in the study scheduled an appointment with the author.[3] During the interview the objectives of the study were explained and women signed a consent form that detailed the requirements of the study and their rights as participants. Women who consented to participate signed a medical authorization form allowing the author access to their medical file (see Appendix C for consent form and medical authorization form).

At the end of the initial interview, the day of the woman's current menstrual cycle and the anticipated date of IVF-ET were recorded so that women could be informed when to begin daily monitoring using the DRK. A detailed explanation on how to complete the DRK was also provided at this time. At the end of the interview, women were given the battery of five

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[3] All appointments were scheduled for Saturday mornings between 8 AM and noon, a convenient time for women because most (88%) were employed.

questionnaires to be completed in the following week and returned in the stamped, pre-addressed envelope provided. On average, women began the IVF-ET cycle 1.83 months ($\underline{SD}$=1.44) after the interview. There was no significant difference between the Non-pregnant and Pregnant groups on interval of time between the interview and the IVF-ET cycle ($\underline{t}$(40)=.01, $\underline{p}$ > .05).

Women completed the DRK for one complete IVF-ET cycle, starting from the first day of GnRH-a administration until the third day following the pregnancy test. This format ensured that daily reactions were available for each stage of IVF-ET including reactions to the success or failure of treatment. Women completed the DRK on a daily basis and mailed the form every week in the provided stamped, pre-addressed envelopes. The author kept track of incoming sheets on a weekly basis and called women if the DRK was not received or late. Three days after the pregnancy test, women completed the retrospective and STAI-state questionnaires and mailed these in the provided pre-addressed, stamped envelope. Women were not contacted after the Retrospective Questionnaire had been received unless a follow-up was deemed necessary at the time of the interview (n=3) or women made a request with clinic staff (n=2).

Women were assigned to their respective groups based on the results they received from their first pregnancy test (biochemical) carried out 14 days after embryo transfer. Pregnancy was established by the presence of at least 25 i.u./L of beta-hCG in the blood sample. The pregnancy rate is substantially higher in this study (40.5%) than that of national estimates (16.3%) (SART-AFS, 1993) because national estimates are based on the clinical pregnancy rate per stimulated cycle, whereas in this study the pregnancy rate is based on biochemical pregnancies per embryo transfer. However, the pregnancy rate

in the study remained high when using the same ratios: clinical pregnancy (n=16) per stimulated cycle (n=51) in the present study was 31.4%, whereas the live birth rate was 21.6% (n=11). Possible reasons for the differential pregnancy rate include such factors as the hormonal regime used at the clinic where subjects were recruited, technical experience (SART, 1993) and other factors not examined in this study.

A subsample of women was also asked to complete the DRK for one complete menstrual cycle without treatment prior to IVF-ET. In total, 50.0% (n=12) of the Non-pregnant women and 55.5% (n=10) of the Pregnant group completed a no-treatment cycle of daily monitoring prior to IVF-ET. It was not possible to obtain a no-treatment cycle for all the sample because some began the IVF-ET cycle on the first day of the menstrual cycle that followed the interview. For the no-treatment cycle, women completed the DRK from the first day of menstrual bleeding until the third day of the following menstrual cycle. Daily reactions during the no-treatment month of monitoring were used as baseline data for reactions experienced during the menstrual cycle.

Data analysis

The analyses in this study consisted primarily of mixed (between-within) analyses of variance (ANOVA) and multiple regression analyses. The statistical approach taken for ANOVA will be presented first, followed by a discussion of the multiple regression analyses. Because power formulas are not readily available for mixed ANOVA designs (Stevens, 1992), it was necessary to estimate power for these analyses from programs for between-subjects ANOVA (Borenstein & Cohen, 1988) and those for single group within-subjects ANOVA (Stevens, 1992). Based on these calculations (using:

n=42, alpha=.05, effect size (f=.25), and moderate correlations between levels of the repeated measures), power for the ANOVAs used in this study was estimated to be between .71 and .82, which is within an acceptable range for psychological studies (Rossi, 1990).

The DRK daily scores provided more than 1, 400 data points per subject. In order to reduce data to a more manageable size, daily scores were converted into average scores in two ways. In order to compare the daily scores of those Non-pregnant and Pregnant women who had completed a no-treatment month of monitoring, daily scores were computed into average scores for each phase of the menstrual cycle: follicular, ovulatory, luteal and menstrual. The ovulatory phase was identified by counting back 14 days from the first day of menstrual bleeding. Days 13-15 were considered to be the ovulatory phase. The menstrual phase consisted of the first day of menstrual bleeding and the two subsequent days. The follicular phase was identified as the days preceding the ovulatory days, whereas the luteal phase consisted of those days between the follicular and menstrual phase. These average phase scores were computed for the distress subscale[4] and each of the physical and behavioral items.

A similar approach was taken with daily scores for comparisons involving the IVF-ET cycle. Daily scores for <u>distress</u> were computed into average scores for the following stages of the IVF-ET process: hormonal suppression (GnRH-a), hMG administration-only, hMG-plus, ovulation induction (hCG), oocyte retrieval, embryo transfer, week one and week two of the waiting period after transfer, and pregnancy test. The stage of hMG-only consisted of those days when women received hMG but did not have blood

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[4] For the distress subscale, phase averages were first computed on the 11 individual items and the average of these scores was used as distress.

tests to determine its dosage or ultrasounds to monitor maturing follicles. The hMG-plus stage refers to hMG administration days when blood tests and ultrasounds were used. Although hMG is administered concurrently with GnRH-a, only the term hMG was used to refer to these stages to simplify identification on Tables and Figures. Pregnancy test days consisted of the day of the pregnancy test and the two subsequent days. The various stages were identified by the treatment codes women indicated on the DRK.

Preliminary analyses indicated that such a breakdown of stages was not necessary for most of the physical and behavioral items. Thus daily scores for items within these subscales were averaged into the following stages: hormonal suppression, ovarian stimulation (all days of hMG administration), ovulation induction, oocyte retrieval-embryo transfer, two week waiting period and pregnancy test. As was the case for the no-treatment month of monitoring, averages were computed on an individual basis because the number of days within each stage varied across women. Scores for all these averages varied from 0 ("symptom not present") to 3 ("severe - efficiency of performing some daily tasks is markedly reduced"). The average scores were used as dependent variables in the ANOVAs.

The assumptions of normality, homogeneity of variance and sphericity required for mixed design ANOVA were verified. The dependent variables (average scores) were moderately positively skewed for all stages except pregnancy test where distributions were normal. Because the skewness was comparable in both groups, transformations were not undertaken since these would not appreciable have affected the results of ANOVA (Tabachnik and Fidell, 1989, p. 84).

The assumption of homogeneity of variance was met in most cases in that the ratio of largest to smallest group variance did not exceed 3:1(Keppel,

1991, p. 106). The only exception was for the stage of pregnancy test where scores for the Non-pregnant group were much more variable than those for the Pregnant group. Because of this discrepancy the assumption of sphericity was violated. To adjust for this violation, Greenhouse-Geisser probability values were used to assess F-ratios for all main and interaction effects in analyses as recommended by Stevens (1992, p. 448). This adjustment makes the analyses more conservative because it reduces the degrees of freedom used to test F-ratios as a function of the severity of the violation of sphericity.

The approach used for the analysis of variance was that recommended by Keppel (1991, p. 249). Significant main effects were followed up with simple comparisons, whereas significant interactions were followed up with simple main effects tests. Because of the conservative nature of this approach and because of the limited sample size, Bonferroni-corrections were not applied (Keppel, 1991, p. 247) since these would undermine the power of the statistical analyses carried out (Sedlmeier & Gigerenzer, 1989). Because the assumption of spherecity was violated, follow-up tests were based on separate rather than pooled error terms (Keppel, 1991, p. 383-384).

Multiple regression analyses were used to examine predictors of treatment distress at each stage of the IVF-ET process. In all cases predictors were entered together as a single block (simultaneous or direct entry). Power calculations were based on: n=40, 3 or 4 predictors, medium effect size (Multiple R^2 =.25), and alpha =.05. Based on these criteria, power for the regressions was estimated to be .79 or .84 depending on the number of predictors entered into the equation (Borenstein & Cohen, 1988). As recommended by Tabachnik and Fidell (1989, p. 129) the ratio of predictor variables to number of subjects did not exceed 10:1 in any of these regressions. The statistical assumptions underlying multiple regression analyses

(linearity, homoscedasticity and normality of residuals) were examined. The only problem identified was non-normality of residuals due to the moderate skewness of the dependent variables. Logarithmic transformations were applied to improve skewness of variable distributions. However, because these transformations did not affect the results of the regressions, original scores were used.

Results

<u>Overview</u>:

The data were analyzed in four parts. The analyses in the first part compared the Non-pregnant and Pregnant groups on variables assessed prior to IVF-ET. In the second part, women's emotional, physical and behavioral reactions during IVF-ET as measured by the DRK were examined. Comparisons between the two groups on biological data were also computed in this section. The third part of the analyses examined women's reactions to IVF-ET failure and their recall of treatment stress. The fourth part of the analyses focused primarily on predictors of treatment distress at each stage of the IVF-ET process. Figures were used when these were the most appropriate format for data presentation. However, Tables presenting the means and standard deviations (and significance tests) for these Figures are provided in Appendix D and E (Tables in Appendix D are ordered by the number corresponding to each of the Figures in text).

I. <u>Psychosocial profile prior to IVF-ET</u>

A. <u>General functioning</u>:

The Pregnant and Non-pregnant groups were compared on marital functioning (MAS) state and trait anxiety (STAI), coping style (MBSS) and

social desirability (SDS) using independent t-tests. As shown in Table 4 significant differences were not obtained on any of these measures.

Sample scores on the MAS, STAI and SDS were compared to norms to determine whether infertile women scored differently. To compute this analysis difference scores were calculated between the combined sample score and the normative score for these measures and these difference scores werecompared to a constant of zero using ANOVA. If the infertile sample scored differently than norms then their difference scores would differ from the constant of zero. As has been reported previously (Mazure, Takefman, Milki, Lake-Polan, 1992), infertile women in this study reported greater marital satisfaction and compatibility than the normative sample of happily married couples ($\underline{F}(1, 41)=35.45$, $\underline{p} < .001$) and scored significantly higher on the measure of social desirability than did the normative sample of undergraduates ($\underline{F}(1, 41)=31.22$, $\underline{p} < .001$). Scores for the combined sample did not differ from those of adult working women on the STAI-Trait ($\underline{F}(1, 41)=.05$, $\underline{p} > .10$) or State anxiety ($\underline{F}(1, 41)=.15$, $\underline{p} > .10$) inventories. Combined sample scores on the MBSS-Monitoring scale were compared to those on the MBSS-Blunting scale using a paired t-test. The t-test revealed that women in this sample relied primarily on information-seeking as a way of coping with stressful situations ($\underline{t}(41)=11.12$, p < .001).

B. Infertility-specific functioning:

A multivariate analysis of variance (MANOVA) was computed comparing the Non-pregnant and Pregnant groups on the life domains most commonly affected by infertility: couple communication and commitment, sexual relationship, family and social relationships and self-esteem. The multivariate F-test for the Group effect was not significant

Table 4

Means (SD) for psychological variables as a function of Pregnancy group

| | Group | | |
	Not Pregnant (n=24)	Pregnant (n=18)	t(40)
MAS - Marital adjustment	117.46 (10.5)	119.94 (12.7)	.68
STAI - Trait anxiety	36.88 (9.9)	35.97 (10.2)	.28
STAI - State anxiety	38.34 (12.3)	34.80 (8.5)	1.04
MBSS - Monitoring	8.54 (2.4)	9.11 (2.5)	.74
MBSS - Blunting	3.08 (1.4)	2.33 (1.9)	1.44
SDS - Social desirability	20.68 (4.5)	20.72 (4.7)	.10

Note. None of the t-values were significant.

(Pillais=.19: F(5, 36)=1.64, p > .05). In order to determine whether the reported effects of infertility were significantly positive or negative, difference scores between the combined sample score and the "no effect" point on the domain Likert-scales were computed. These difference scores were compared to a constant of zero. If women reported significant positive or negative effects, then the sample scores would be above or below the "no effect" point. The multivariate effect was significant for this comparison (Pillais=.41: F(5, 37)=5.22, p < .01). As shown in Figure 1, univariate F-tests showed that women reported that infertility had had a significant positive effect on couple communication and commitment. In contrast, women reported a significant negative effect on family and social relationships and a marginally negative effect on quality of the sexual relationship.

A second MANOVA was computed on measures of infertility distress. These included the IFQ, childbearing focus which measures the extent to which having a child is a major focus of one's life and women's report of how well they coped with the strains of infertility. The multivariate F-test was not significant (Pillais=.11: F(3, 38)=1.51, p > .10). Mean scores on the IFQ (M=2.30, SD=.57) were below the "distress" range reported by Bernstein et al. (1985) and in the moderate range for childbearing focus (M=13.62, SD=4.05). On average, women reported coping well with the strains of infertility (M=4.12, SD=.86).

C. Treatment expectations

During the interview, women were asked a number of questions regarding their preparation for and expectations about IVF-ET treatment. Specifically, they were asked to indicate the extent to which they felt well-informed about 1) the procedures involved in IVF-ET, and 2) the risks

Figure 1. Impact of infertility on various domains.
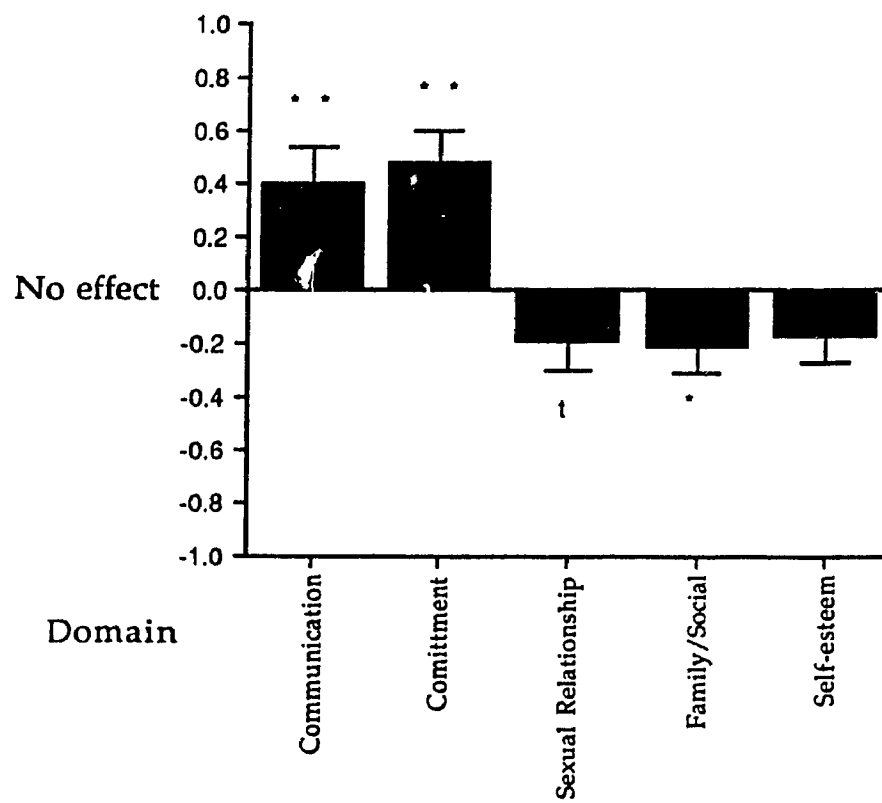
t p less than .10
** p less than .001

associated with the procedures and the potential side effects of medication. They also rated how nervous and enthusiastic they felt about doing IVF-ET and the extent to which they felt they would be depressed or disappointed if it failed. Finally, women indicated their chances of success with IVF-ET according to their doctor[5] and according to their own beliefs. In order to compare these variables in the Non-pregnant and Pregnant groups, a 2 (Group) x 2 (Scale) MANOVA was computed using Scale as a repeated measure. The multivariate effect of Group (Pillais=.06: $F(4, 37)$=.64, p > .05) and the Group X Scale interaction (Pilla's=.07: $F(4, 37)$=.65, p > .05) were not significant. However, the multivariate effect of Scale was significant (Pillais=.70, $F(4, 37)$=21.94, p < .001). Means and standard deviations for these variables are presented in Table 5. Univariate F-tests for the Scale effect showed that women felt better informed about the procedures involved in IVF-ET than of its risks, felt more enthusiastic than nervous about doing IVF-ET, felt more optimistic than their doctors and expected to be more disappointed than depressed if IVF-ET failed.

Because SDS scores were higher in this infertile sample than in the normative sample, this variable was correlated with the measures of general functioning, infertility distress and expectations about IVF-ET. Social desirability correlated most strongly with the measures of distress (i.e., STAI-Trait and State scales, IFQ, childbearing focus) with those scoring more highly on the SDS reporting less distress (correlations ranging from: r=-.26 to -.53), which is consistent with previous reports (Paulhus, 1984). Although the group difference was not significant on the SDS, all analyses involving the distress variables were repeated with social desirability as a covariate. Results

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[5] Doctor's estimate based on patient recall.

Table 5

Means (SD) for variables measuring preparation for and expectations about
IVF-ET for the combined sample (n = 42)

Scale	Mean (SD)	$F(1, 40)^a$
Information		
• IVF-ET procedures	4.17 (1.06)	
• IVF-ET risks/side · < cts	2.95 (1.45)	22.74***
Reactions to IVF-ET		
• Nervous	2.86 (1.32)	
• Enthusiastic	3.83 (1.08)	15.85***
Estimates of success		
• Doctor's^b	32.14 (10.95)	
• Personal	55.17 (27.17)	25.55***
Anticipated reactions to IVF-ET failure		
• Disappointment	4.43 (.80)	
• Depression	3.21 (1.28)	45.04***

[a] F-ratio compares the two Scales under each heading

[b] Doctor's estimate as reported by the patient

***$p \leq .001$

from these analyses did not differ from those presented and mean values adjusted for social desirability were not markedly different from the unadjusted means.

In summary, Non-pregnant and Pregnant women were functioning well prior to IVF-ET particularly with regard to their marital relationships. Both groups of women reported some infertility distress in particular with regard to their sexual relations and social relationships. Despite these negative effects, women reported coping well with the strains of infertility. Both groups felt well prepared for IVF-ET and had a positive outlook on it.

D. Reactions during the no-treatment menstrual cycle

The Non-pregnant and Pregnant groups were also compared on reactions experienced during a menstrual cycle without treatment. As mentioned previously, for these comparisons average scores were created for the follicular, ovulatory, luteal, and menstrual phases of the cycle. Preliminary analyses on the data revealed that two subjects, one in each group, were outliers in both the No-treatment and IVF-ET cycles of monitoring. Because these subjects were extreme outliers on all phases/stages (5-8 standard deviations from the mean of their respective groups) they were dropped from subsequent analyses involving reactions during the No-treatment or IVF-ET cycles. Thus sample sizes for analyses involving the no-treatment month are based on 11 Non-pregnants and 9 Pregnants. The only dependent variables analyzed were average scores for the distress subscale, fatigue, relationship variables (affection, good talk and arguments with spouse), socializing and optimism. Other items of the physical and behavioral subscale were not analyzed because they showed either zero variance or were

not relevant (estrogen-related scores). The analyses consisted of a series of 2 (Group) x 4 (Phase) ANOVAs with Phase as repeated measure.

A significant Phase main effect was obtained for distress scores ($F_{(3, 54)}$=4.87, p < .05). As shown in Figure 2, simple comparisons between phases showed that the luteal phase was significantly less stressful than the follicular phase ($F_{(1, 19)}$=21.251, p < .001) and ovulatory phase ($F_{(1, 19)}$=8.70, p < .001). Neither the main effect of Group ($F_{(1, 18)}$=.08, p > .05) or Group X Phase interaction ($F_{(3, 54)}$=2.33, p > .05) was significant.

A significant main effect of Phase was also obtained for fatigue ($F_{(3, 54)}$=5.65, p < .01). Simple comparisons between phases were computed and, as shown in Figure 3, women reported significantly less fatigue during the luteal phase than during the follicular ($F_{(1, 19)}$=25.10, p < .001) or menstrual phases ($F_{(1, 19)}$=4.03, p < .001) of the cycle. In addition, women reported significantly more fatigue during the menstrual phase of the cycle as compared to the ovulatory phase ($F_{(1, 19)}$=4.79, p < .05).

Significant main effects of Phase were obtained for affection with partner ($F_{(3, 54)}$=9.73, p < .001), good talk with partner ($F_{(3, 54)}$=6.63, p < .001) and socializing ($F_{(3, 54)}$=5.17, p < .01). Means and standard errors for these variables are presented in Figure 4. The pattern of changes across the no-treatment cycle was similar for the three variables. Simple comparisons between phases showed that affection was significantly lower during the luteal phase than during the follicular ($F_{(1, 19)}$=24.50, p < .001), ovulatory ($F_{(1, 19)}$=28.84, p < .001) and menstrual phases ($F_{(1, 19)}$=5.02, p < .05) of the cycle. In addition, affection was higher during the ovulatory phase than during the follicular ($F_{(1, 19)}$=11.63, p < .01) and menstrual phases ($F_{(1, 19)}$=7.84, p < .01) of the cycle. As was the case for affection, simple comparisons for good talk with partner showed that women reported fewer talks with their partner

Figure 2. Mean level of distress (± SE mean) as a function of Pregnancy group and Phase of the no-treatment menstrual cycle.
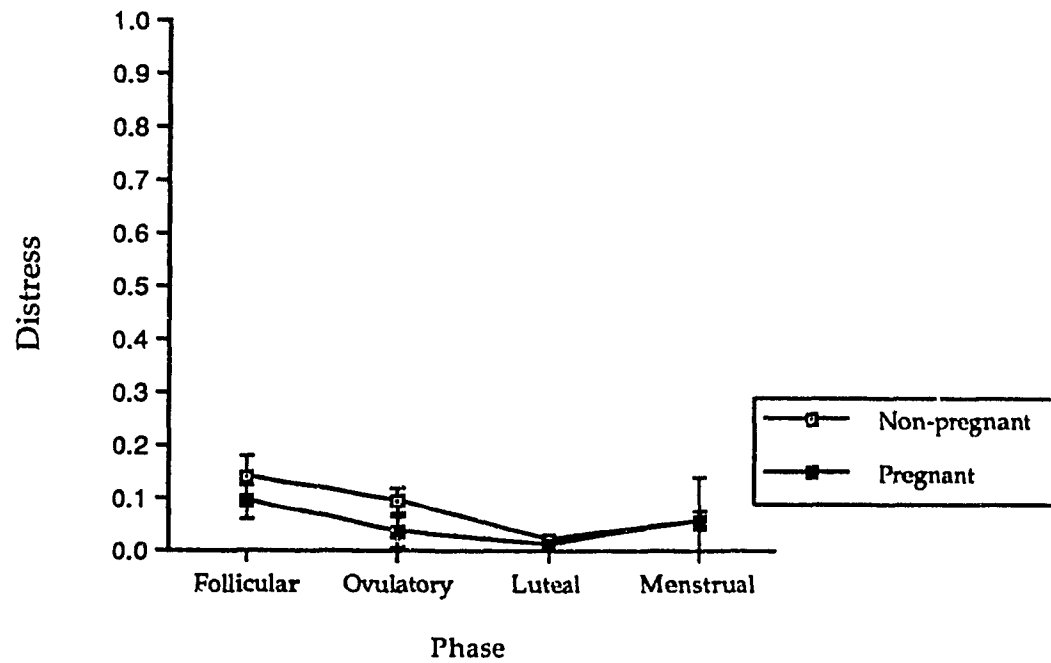
Figure 3. Mean level of fatigue (± SE mean) as a function of Phase of the no-treatment menstrual cycle.
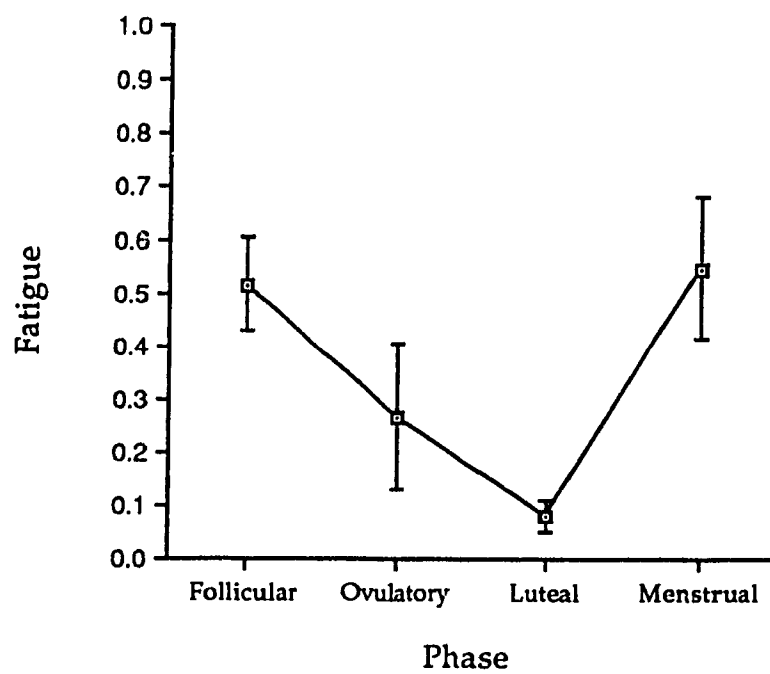
Figure 4. Mean level of affection and good talk with partner, and socializing
(± SE mean) as a function of Phase of the no-treatment menstrual cycle.
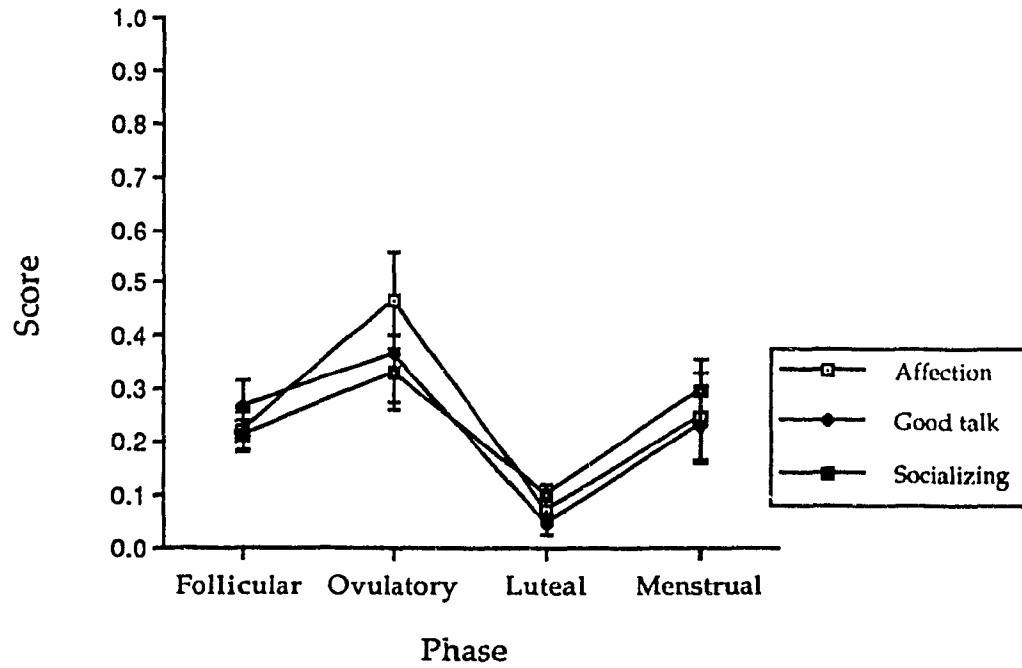
during the luteal phase of the cycle as compared to the follicular ($F(1$, 19)=28.52, $p < .001$), ovulatory ($F(1, 19)$=16.65, $p < .001$) and menstrual phases ($F(1, 19)$=7.34, $p < .05$). Simple comparisons revealed that socializing with friends was significantly lower during the luteal phase than during the follicular ($F(1, 19)$=11.22, $p < .01$), ovulatory ($F(1, 19)$=12.67, $p < .01$) and menstrual phases of the cycle ($F(1, 19)$=10.75, $p < .01$).

A significant Group x Phase interaction was obtained for arguments with spouse ($F(3, 54)$=3.58, $p < .05$). Simple main effects of group at each phase revealed that the interaction was due to a marginally greater number of arguments in the Non-pregnant group during the ovulatory phase (M=.152, SD=.17) as compared to the Pregnant group (M=.037, SD=.11) ($F(1, 18)$=3.17, $p < .10$). The main effect of Group ($F(1, 18)$=.28, $p > .05$), Stage ($F(3, 54)$=2.24, $p > .05$) or Group X Stage interaction ($F(3, 54)$=2.44, $p > .05$) were not significant for optimism. Finally, a significant main effect of Stage was also obtained for intercourse frequency ($F(3,54)$=6.13, $p < .001$). Simple comparisons among phases revealed that intercourse frequency was higher during the ovulatory phase as compared to the follicular ($F(1,19)$=8.12, $p < .01$), luteal ($F(1,19)$=5.33, $p < .05$) and menstrual phases ($F(1,19)$=7.56, $p < .05$).

In summary, the Non-pregnant and Pregnant groups were comparable in terms of their reactions during a menstrual cycle without treatment. As compared to other phases, the luteal phase was associated with the lowest incidence of symptom reports: less distress, fatigue, affection and discussion with spouse and socializing. The frequency of intercourse was higher during the ovulatory phase of the cycle as compared to other phases and the Non-pregnant group reported more arguments with their spouse during this phase.

II. Reactions to IVF-ET

A. Emotional reaction:

As mentioned previously, average distress scores were created for hormonal suppression, hMG-only, hMG-plus (blood tests and ultrasounds), ovulation induction, oocyte retrieval, embryo transfer, week one and two of the waiting period and pregnancy test. Comparisons during the IVF-ET cycle are based on sample sizes of 23 for the Non-pregnant group and 17 for the Pregnant group. A 2 (Group) x 9 (Stage) ANOVA was computed (with Stage as a repeated measure) to compare distress level in the Non-pregnant and Pregnant groups. The main effects of Group and Stage were significant. However, these effects were qualified by a significant Group x Stage interaction ($\underline{F}(8, 304)=13.56$, $\underline{p} < .001$). The simple effects of pregnancy group at each stage of the IVF-ET process were examined. As shown in Figure 5, the two groups differed significantly at all stages of IVF-ET except during hormonal suppression, hMG-only, and the two week waiting period. In each case, the Non-pregnant group reported more distress than the Pregnant group.

B. Physical reactions:

The physical reactions of the Non-pregnant and Pregnant groups were also examined at each stage of the IVF-ET process. Because the item weight loss showed zero variance at all stages after hormonal suppression it was not analyzed. All other items, including those of estrogen-related symptoms were analyzed. In the case of dizziness, nausea, constipation and fatigue, the stages of oocyte retrieval and embryo transfer were analyzed separately because preliminary analyses showed these to differ.

Figure 5. Mean level of distress (± SE mean) as a function of Pregnancy group and Stage of the IVF-ET process.
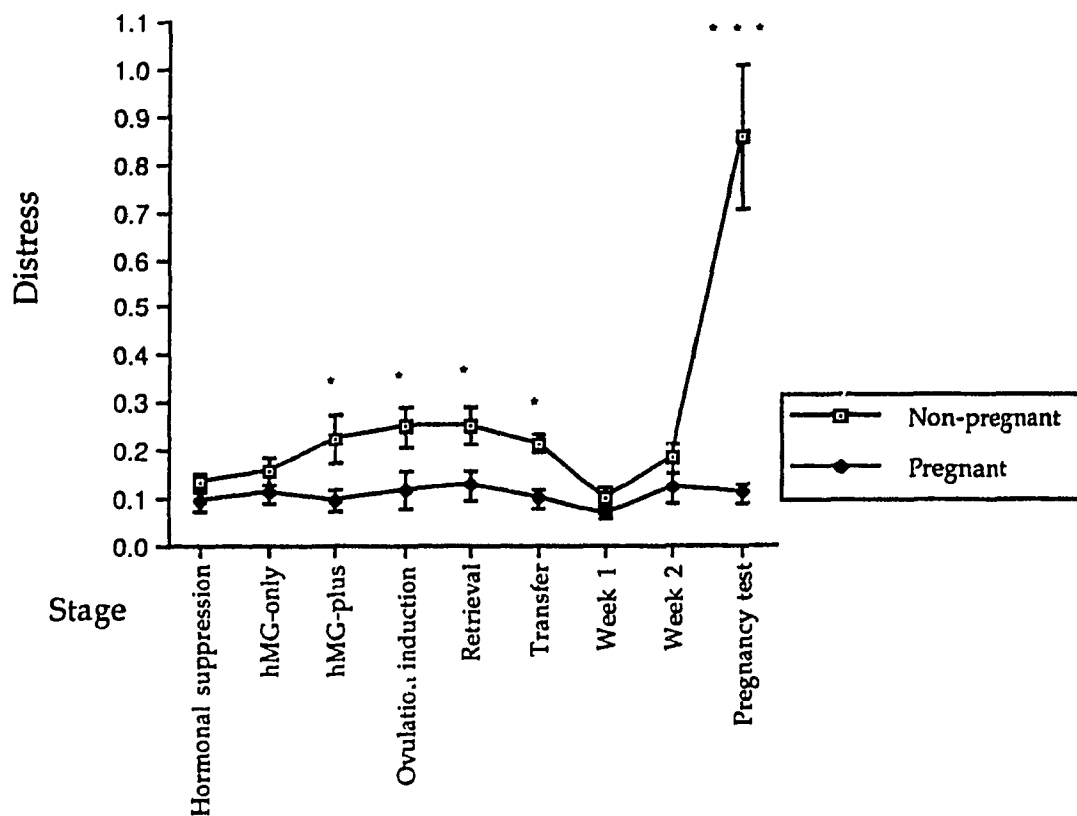
* p less than .05

** p less than .001

Main effects of Stage were obtained for estrogen-related symptoms (F(5, 190)=20.72, p < .001), constipation (F(6, 228)=4.01, p < .05) and fatigue (F(6, 228)=7.45, p < .001). As shown in Figure 6, Estrogen-related symptoms were highest during the phase of oocyte retrieval-embryo transfer and lowest during hormonal suppression and ovarian stimulation. Simple comparisons showed that constipation was generally higher during embryo transfer and the waiting period than all other stages (see Figure 7). Finally, as shown in Figure 8, the stages associated with the most fatigue were ovarian stimulation, ovulation induction and oocyte retrieval. Women reported significantly more fatigue during these stages than during hormonal suppression, embryo transfer, waiting period and pregnancy test. In addition, women experienced significantly less fatigue during the waiting period than during the stage of pregnancy test. A main effect of Group was also obtained for fatigue (F(1, 38)=4.86, p < .05) showing that the Non-pregnant group experienced more fatigue (M=.797, SD=.451) throughout the IVF-ET cycle than the Pregnant group (M=.493, SD=.393).

Group x Stage interactions were obtained for increased appetite (F(5, 190)=4.70, p < .01) and decreased appetite (F(5,190)=2.39, p < .10). Because these two variables provide the same information, only the interaction for decreased appetite will be examined. Comparisons between the Non-pregnant and Pregnant groups at each stage of the IVF-ET process were computed. These revealed that the Non-pregnant group reported a decrease in appetite at the time of the pregnancy test (M=.457, SD=.65) as compared to the Pregnant group (M=.103, SD=.25) (F(1, 39)=5.66, p < .05).

A significant Group x Stage interaction was obtained for dizziness (F(6, 228)=4.04, p < .05). The simple effects of Group at each stage were examined. As shown in Figure 9, The Non-pregnant group experienced significantly

Figure 6. Mean level of estrogen-related symptoms (± SE mean) as a function of Stage of the IVF-ET process.
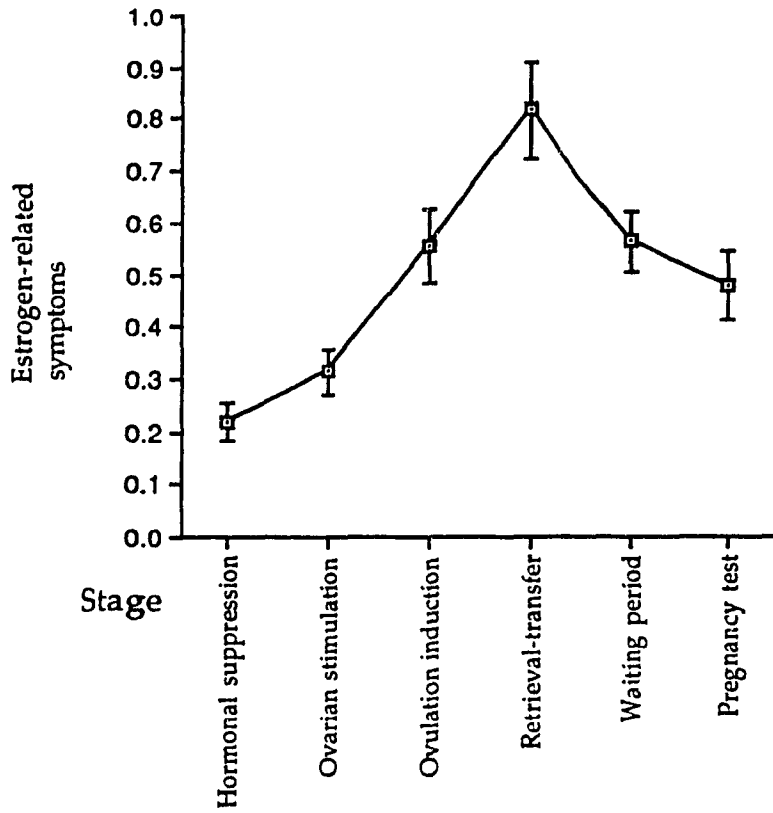
Figure 7. Mean level of constipation (± SE mean) as a function of Stage of the IVF-ET process.
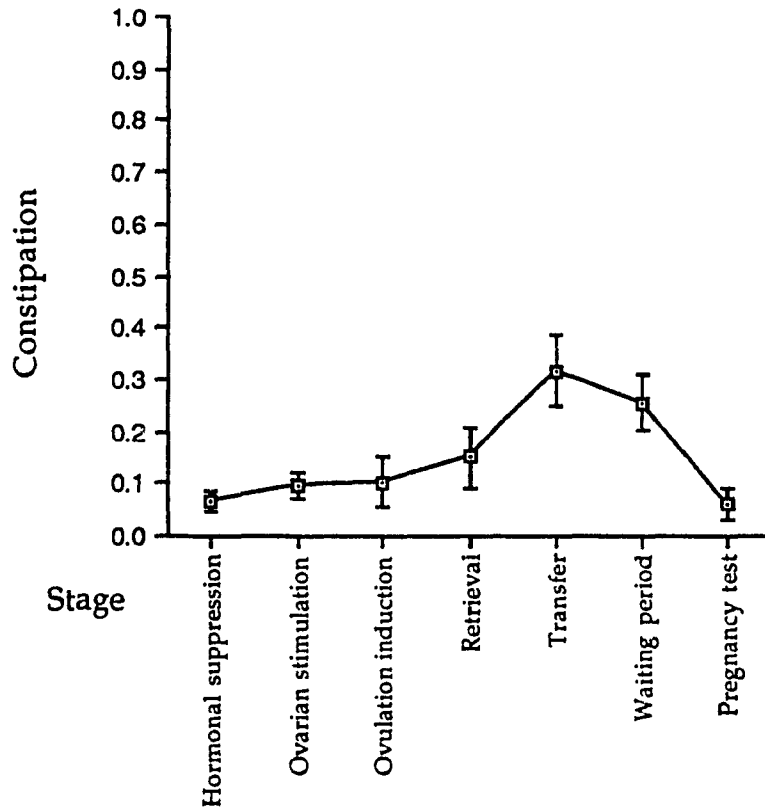
Figure 8. Mean level of fatigue ($\pm$ SE mean) as a function of Stage of the IVF-ET process.
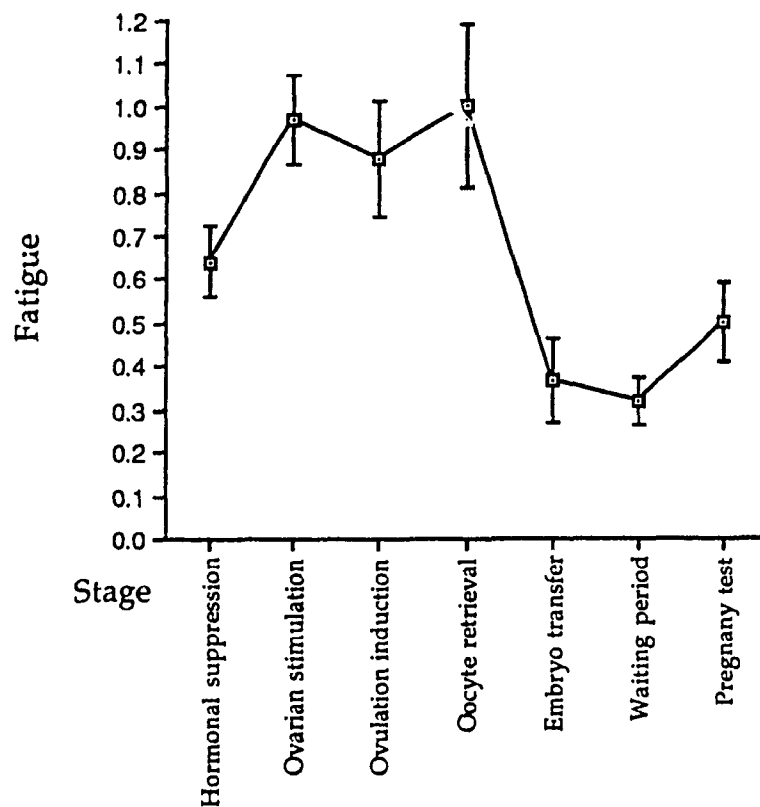
Figure 9. Mean level of dizziness (± SE mean) as a function of Pregnancy group and Stage of the IVF-ET process.
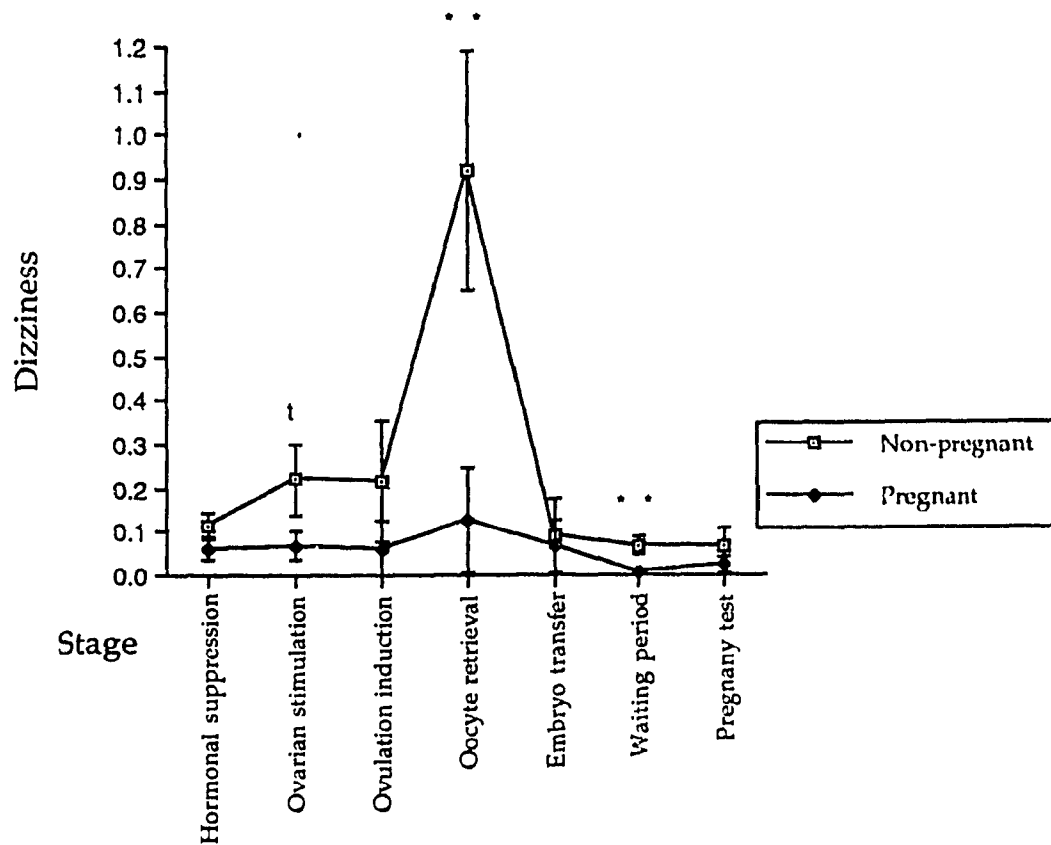
· t p less than .10

** p less than .01

more dizziness during oocyte retrieval and the two week waiting period than did the Pregnant group. In addition, the Non-pregnant group experienced marginally more dizziness during ovarian stimulation.

A significant Group x Stage interaction was also obtained for headaches ($F(5, 190)=3.83$, $p < .01$). Comparisons between the pregnancy groups showed a significant difference during ovarian stimulation, waiting period and time of pregnancy test. As shown in Figure 10, the Non-pregnant group reported more headaches than the Pregnant group at each of these stages. Significant effects were not obtained for nausea, weight gain or insomnia.

In summary, physical reactions were consistent with hormonal administration and/or the medical procedures involved at the various stages. As expected, severity of estrogen-related symptoms (due to hMG administration) rose steadily and peaked at the time of oocyte retrieval with a decrease after embryo transfer. Similarly, constipation was higher during the initial weeks of progesterone supplements. For both groups fatigue was highest during those stages when daily attendance at the clinic was required (i.e., ovarian stimulation, ovulation induction and oocyte retrieval-embryo transfer). Group differences were observed for fatigue, dizziness, headaches, and appetite changes.

C. Behavioral reactions:

Significant effects were not obtained for pregnancy dreams, arguments with spouse and lack of concentration at work. A marginally significant Group x Stage interaction was obtained for optimism ($F(5, 190)=2.01$, $p < .10$). Comparisons between the Non-pregnant and Pregnant groups at each stage of the IVF-ET process revealed that the Non-pregnant group was marginally more optimistic during hormonal suppression and significantly less

Figure 10. Mean level of headaches ($\pm$ SE mean) as a function of Pregnancy group and Stage of the IVF-ET process.
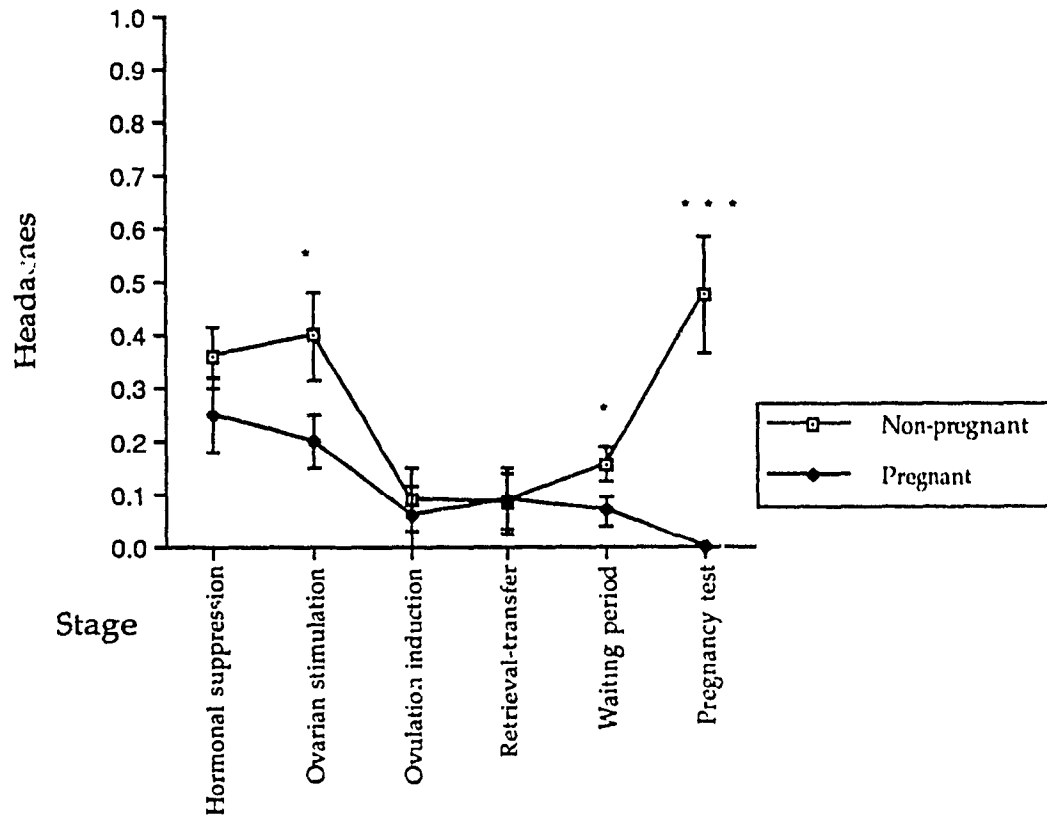
* p less than .05

*** p less than .001

optimistic during the time of the pregnancy test than was the Pregnant group. Means and standard errors for optimism for the pregnancy groups are presented in Figure 11. However, a significant main effect of Stage ($\underline{F}$(5, 190)=11.12, $\underline{p}$ < .01) revealed that for both groups optimism was significantly higher during ovulation induction and oocyte retrieval-embryo transfer than during other stages of the cycle.

Significant main effects of Stage were also obtained for affection with partner ($\underline{F}$(5, 190)=5.11, $\underline{p}$ < .001) and good talk with partner ($\underline{F}$(5, 190)=4.47, $\underline{p}$ < .01). Figure 12 shows that affection was higher during oocyte retrieval-embryo transfer and Pregnancy test stage than at all other stages. Women also reported more talks with their spouse during the Pregnancy test stage than at all other ages as shown in Figure 13. In addition, women reported marginally more talks during the oocyte retrieval-embryo transfer stage than during the waiting period. Significant main effects of Stage were also obtained for socializing ($\underline{F}$(5, 190)=4.32, $\underline{p}$ < .01). Means and standard errors for socializing as a function of stage are presented in Figure 14. Women reported socializing significantly less during oocyte retrieval and embryo transfer than during all other stages. Finally, mean scores for feeling pregnant were higher on the day of embryo transfer ($\underline{M}$=.079, $\underline{SD}$=.266) and the waiting period ($\underline{M}$=.131, $\underline{SD}$=.229) than during preceding stages (M=0). An ANOVA could not be computed because of the lack of variance in initial stages.

In summary, there were few differences in the behavioral reactions of the Non-pregnant and Pregnant groups and significant effects were primarily due to the various stages of treatment. For both groups oocyte retrieval-embryo transfer was associated with an increase in optimism, affection and discussion with spouse. Socializing remained constant throughout the cycle with a decrease during oocyte retrieval, a change that was consistent with the

Figure 11. Mean level of optimism (± SE mean) as a function of Pregnancv
group and Stage of the IVF-ET process.
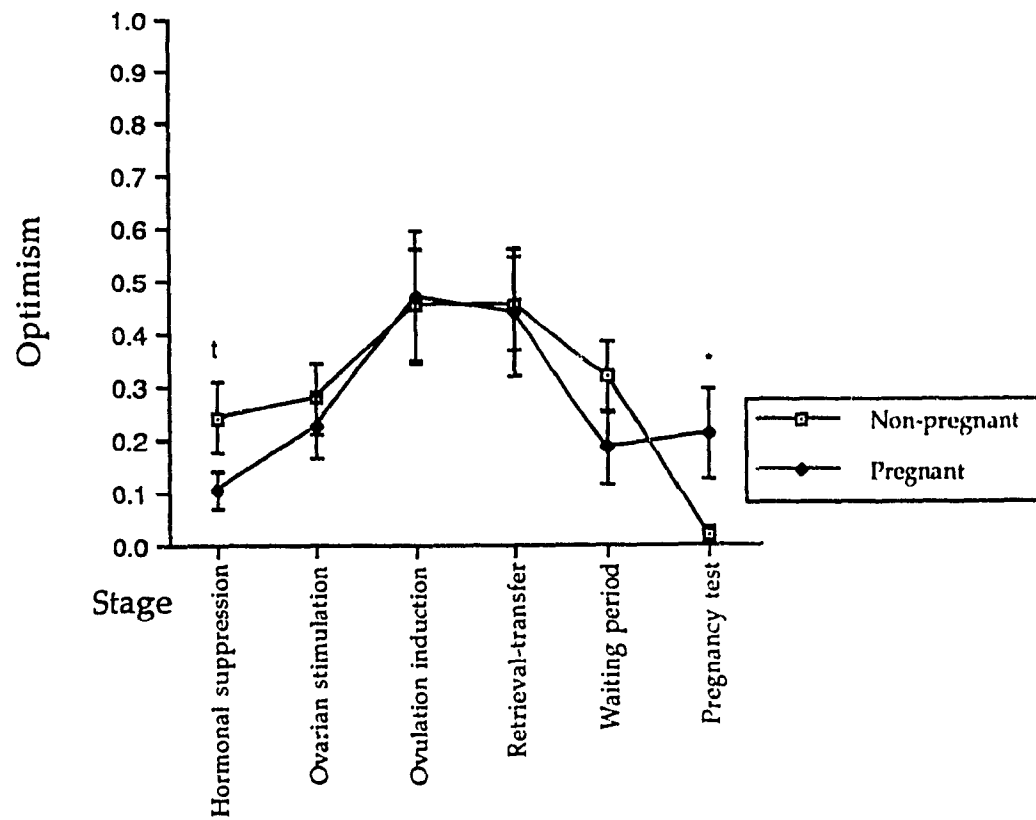
t less than .10

* p less than .05

Figure 12. Mean level of affection ($\pm$ SE mean) as a function of Stage of the IVF-ET process.
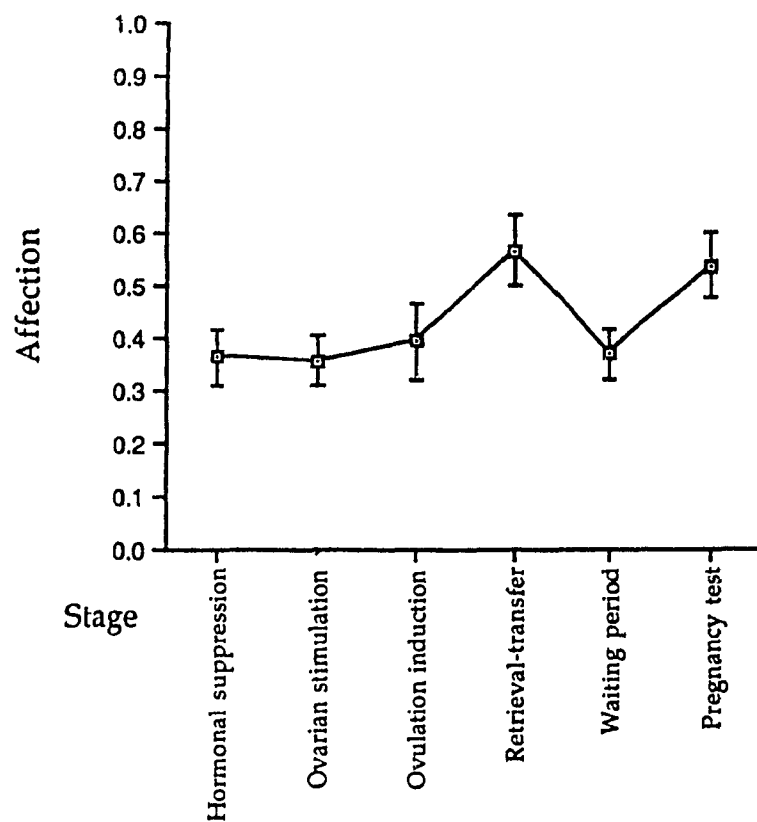
Figure 13. Mean level of good talk with partner (± SE mean) as a function of Stage of the IVF-ET process.
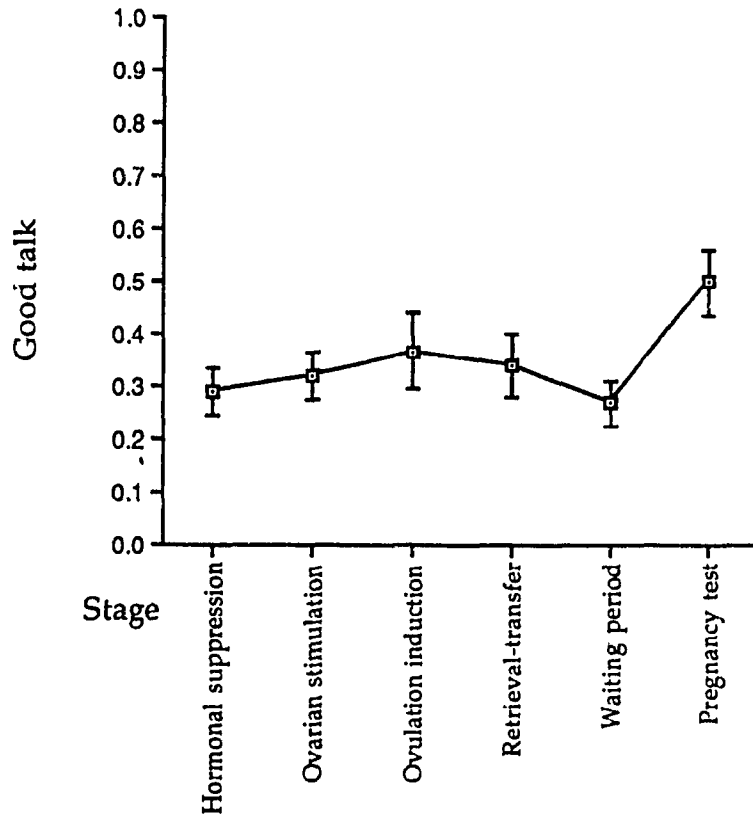
Figure 14. Mean level of socializing (± SE mean) as a function of Stage of the IVF-ET process.
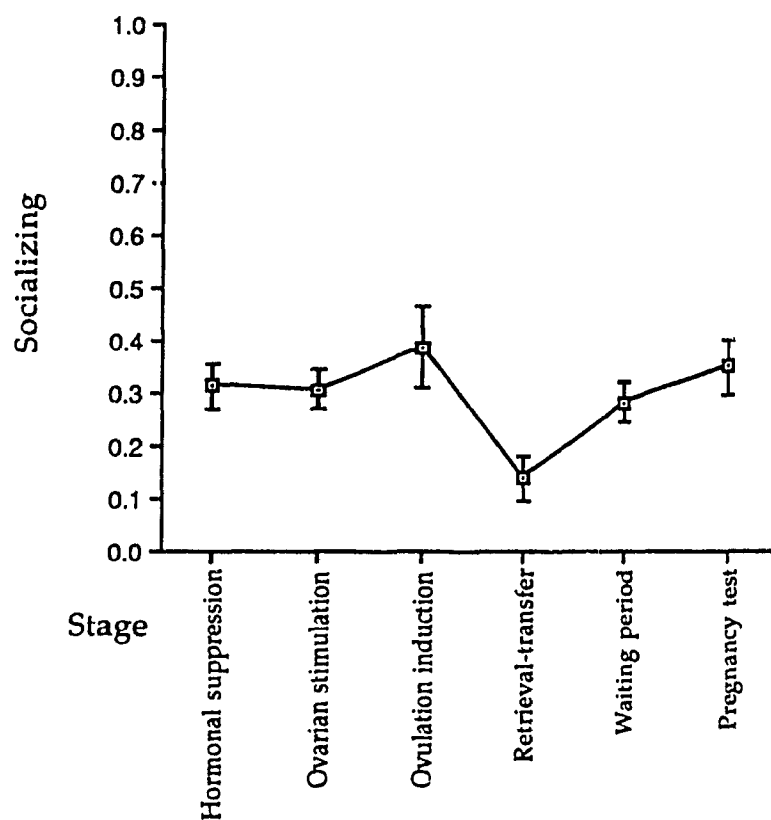
medical procedures involved at this stage. For both groups the stage of pregnancy test was associated with greater feelings of closeness with spouse (affection and good talk). The only group differences observed were that the Non-pregnant group reported slightly more optimism at the start of treatment whereas the Pregnant group reported, as would be expected, more optimism at the time of the pregnancy test.

D. Biological reactions

During the IVF-ET process various biological parameters were used by the medical team to determine the progress of ovarian stimulation and the results of oocyte retrieval and embryo transfer. The Non-pregnant and Pregnant groups were compared on each of these variables through a series of one way MANOVAs. Means and standard deviations for these variables, along with univariate F-tests comparing the two groups are shown in Table 6.

The multivariate F-test for the Group effect comparing the two groups on the number of hMG ampoules used and peak estrogen (E2) levels per maturing follicle was marginally significant (Pillais=.12: $F_{(2,37)}$=2.50, $p < .10$). Univariate F-tests showed that the Non-pregnant group used marginally more hMG ampoules to reach peak E2 levels and had significantly lower peak E2 levels per maturing follicle than the Pregnant group. Figure 15 shows estradiol levels at each of the successive blood tests used to calibrate dosage of hMG. As can be seen from this graph, estradiol levels rose more quickly in the Pregnant (slope=1675.4) than in the Non-pregnant group (slope=979.1) ($t_{(38)}$=2.82, $p < .01$).

A significant multivariate effect of Group was obtained for the MANOVA comparing the two groups on the number of mature and immature eggs retrieved (Pillais=.31: $F_{(2,37)}$= 8.45, $p < .001$). Univariate F-tests

Table 6

Means (SD) for biological variables as a function of Pregnancy group

Variable	Group Not Pregnant (n=23)	Pregnant (n=17)	F (1, 38)
Ovarian stimulation			
No. of hMG ampoules	26.48 (3.4)	24.62 (3.4)	2.95[t]
Peak E2 level (pm/L) per maturing follicle	873.58 (304.2)	684.42 (264.8)	4.41*
Oocyte retrieval			
Immature eggs	1.91 (1.6)	5.00 (2.3)	15.57***
Mature eggs	4.47 (2.5)	7.29 (4.1)	5.15*
Embryo transfer			
No. of embryos	4.52 (2.8)	9.23 (4.3)	17.45***
No. of embryos transferred	2.52 (0.7)	2.94 (0.2)	5.15*
Quality of embryos	40.65 (21.1)	50.47 (11.4)	3.02[t]
Sperm quality			
Volume (ml)	2.34 (1.3)	2.42 (1.3)	.04
Percent motile (grade "A")	40.74 (21.3)	46.88 (22.2)	.69
Count (10^6/ml)	85.35 (53.0)	91.71 (59.2)	.13

[t] $p \leq .10$

* $p \leq .05$

*** $p \leq .001$

Figure 15. Mean estradiol level (± SE mean) as a function of blood test day.
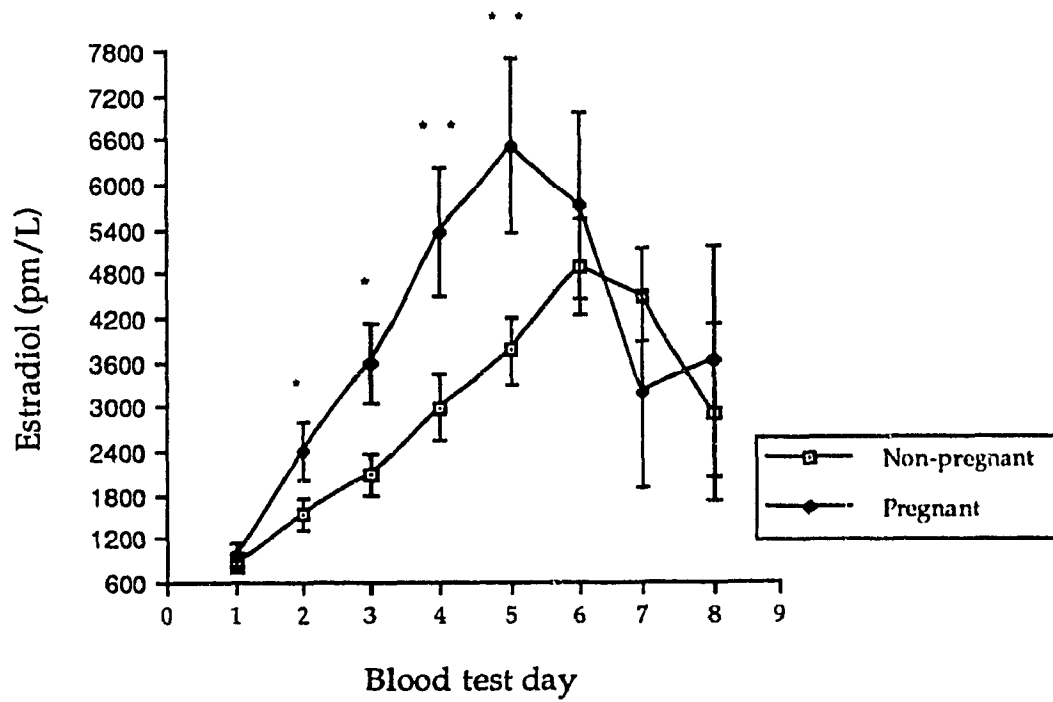
* p less than .05

** p less than .01

showed that the Non-pregnant group had significantly fewer eggs, both immature and mature, than the Pregnant group. A MANOVA comparing the groups on the number of embryos obtained, transferred and the quality of these transferred embryos was significant (Pillais=.34: $F(3,36)=6.06$, $p < .001$). Univariate F-tests showed that fewer embryos were obtained in the Non-pregnant group and fewer were transferred to the uterus than in the Pregnant group. In addition, the quality of transferred embryos was poorer in the Non-pregnant group than in the Pregnant group.

A MANOVA comparing the two groups on semen quality was not significant (Pillais=.02: $F(3,36)=.25$, $p > .10$). The two pregnancy groups did not differ in terms of the volume of semen collected, number of sperm or percent of motile sperm in the sample.

Correlations were computed between biological data collected during ovarian stimulation, oocyte retrieval and embryo transfer and distress scores during those stages. Peak estradiol level (per maturing follicle) was related to distress during ovarian stimulation ($r(40)=.37$, $p < .05$), number of oocytes retrieved with distress during oocyte retrieval ($r(40)=-.30$, $p < .10$), and number of embryos transferred with distress during transfer ($r(40)=-.37$, $p < .10$). The correlations show that poorer values on the biological indicators of progress were associated with greater distress.

III. Reactions to IVF-ET outcome and comparison between retrospective and prospective reports of distress

Three days after the outcome of IVF-ET was known, subjects completed the STAI-State anxiety inventory and rated the stress they experienced at each stage of the IVF-ET process. A 2 (Group) x 2 (Time) ANOVA with Time as repeated measure was computed to compare STAI-State levels prior to and

three days after IVF-ET. The Group x Time interaction was marginally significant ($F(1,38)=2.72$, $p < .10$)). Simple effects of Time at each group revealed that the Non-pregnant group experienced a significant increase in anxiety from pre- to post-treatment ($F(1,21)=7.84$, $p < .01$) whereas the Pregnant group did not ($F(1,16)=.24$, $p > .05$).

One of the objectives of this study was to examine the effect of knowledge of IVF-ET outcome on <u>recall</u> of treatment stress. In order to examine this issue prospective ratings of treatment distress were compared to retrospective ratings. The prospective ratings were those obtained using the distress subscale of the DRK monitoring form whereas the retrospective ratings were those obtained from Likert-type ratings (i.e., "not stressful" to "extremely stressful") in the Retrospective Questionnaire. Because the two sets of ratings were not in comparable units of measurement they were transformed to standardized scores using the pooled within-groups variance estimate (Tabachnik and Fidell, 1989, p. 440). The analysis was a 2 (Group) x 2 (Method) x 4 (Stage) ANOVA with Method and Stage as repeated measures. The four stages were ovarian stimulation, oocyte retrieval-embryo transfer, two week waiting period and pregnancy test.

A significant Method x Stage interaction was obtained ($F(3, 114)=39.58$, $p < .001$). Simple comparisons between the two methods were computed at each stage of the IVF-ET process to determine the source of the interaction in the overall sample. As shown in Figure 16, all women remembered the waiting period as more stressful once they knew the outcome of IVF-ET than when they were awaiting these results as recorded on the daily monitoring form. In addition, a significant main effect of Group ($F(1,38)=16.88$, $p < .001$) showed that regardless of the method of measurement, the Non-pregnant

Figure 16. Mean standardized stress rating (± SE mean) as a function of Method of measurement and Stage of the IVF-ET process.
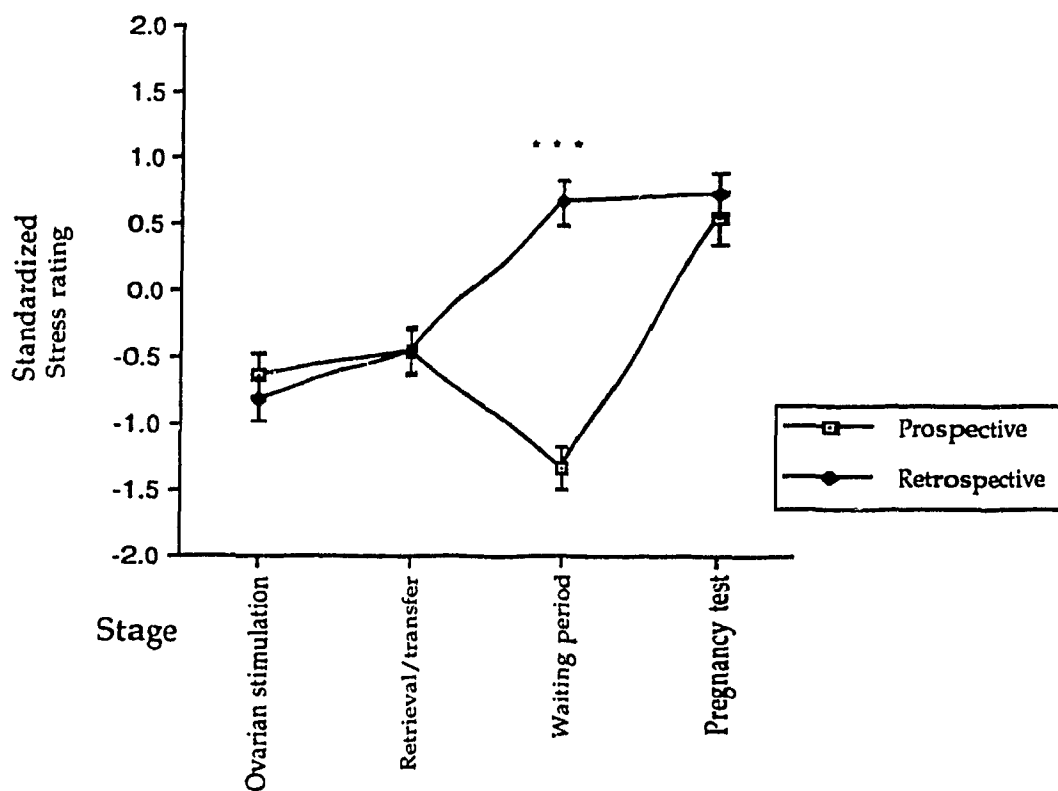
*** p less than .001

group scored higher ($\underline{M}$=.092, $\underline{SD}$=.58) than the Pregnant group ($\underline{M}$=-.654, $\underline{SD}$=.55).

IV. Predictors of emotional reactions during IVF-ET

Multiple regression analyses were used to identify predictors of extent of emotional reactions during IVF-ET. The dependent measures considered for these analyses were the average distress scores at each of the stages of IVF-ET except pregnancy. A regression was not computed for this last stage since distress would most obviously be due to the results obtained. The variables considered as potential predictors were demographic and medical variables, general psychological and infertility specific measures of distress, as well as expectations and feelings about undergoing IVF-ET. Among these, only those predictors that had significant or marginally significant pairwise correlations with the dependent measures were included in the regression analyses (see regression summary Tables). Multiple regression analyses were not computed for the stages of hormonal suppression, ovarian stimulation and ovulation induction because only one or no variables were related to these stages. Marital adjustment (MAS) was the onl· pre-treatment variable found to correlate with distress during ovarian stimulation ($\underline{r}$(40)=-.30, $\underline{p}$ < .10) and ovulation induction ($\underline{r}$(40)=-.30, $\underline{p}$ < .10), and for both lower distress was associated with better marital adjustment. None of the pre-treatment variables correlated with hormonal suppression.

Multiple regression analysis is used to determine whether a set of predictor variables can account for a significant proportion of variance in the dependent measure of interest (Multiple R^2). For the regressions used in this study, variables were entered together in one block in what is referred to as simultaneous-entry (Cohen & Cohen, 1983). This strategy was used because

there was no *a priori* theoretical reason to enter variables in a specific order (hierarchical regression) and because of the statistical problems associated with stepwise regressions computed on small sample sizes. The importance of a predictor variable is based on its unique contribution to multiple R^2 as measured by its semi-partial correlation squared (sr^2). This value as well as the correlation between each predictor and dependent measure are presented in the Tables summarizing the results of the , ression analyses computed. In addition, both the Multiple R^2 and adjusted R^2 values are presented. The latter adjusts for inflation in R^2 due to small sample sizes.

The multiple regressions were significant for each stage examined. Approximately 30% of the variance in distress scores during oocyte retrieval was explained by the set of predictors. Lower distress was associated with older age, shorter duration of infertility, less enthusiasm at the start of IVF-ET and less emphasis on childbearing as a major life goal (see Table 7). Of these, the most important predictor in terms of unique variance was childbearing focus (7.0%). The predictors of distress during embryo transfer were childbearing focus, social desirability and monitoring, accounting for 22% of the variance in distress scores (see Table 7). Unique contributions to R^2 were greatest for social desirability (7.1%) and monitoring (6.0%). Lower distress during embryo transfer was associated with less information-seeking and greater social desirability.

Summary statistics for multiple regressions during the waiting period are presented in Table 8. During the first week of the waiting period, older age, higher social desirability and less information-seeking were associated with less distress. Together the variables accounted for 25% of the variance in distress scores, with social desirability accounting for 10.6% of the explained variance. Lower distress during the second week of the waiting period was

Table 7

Summary statistics for multiple regression analysis predicting distress during oocyte retrieval and embryo transfer

Predictors	Beta	Correlation	sr^2(%)	t
Oocyte retrieval				
Age	-.21	-.31	3.9	1.40
Years infertile	.21	.28	4.4	1.48
Enthusiasm	.14	.29	1.7	.93
Childbearing focus	.30	.45	7.0	1.87[t]

Multiple R^2=.30; Adjusted R^2=.22; F(4, 35)=3.76, p < .05

Embryo transfer				
Childbearing focus	-.01	.31	.0	.06
Social desirability	-.33	-.38	7.1	1.81[t]
MBSS-Monitoring	.28	.34	6.0	1.65[t]

Multiple R^2=.22; Adjusted R^2=.15; F(3, 36)=3.29, p < .05

Note. sr^2=semi-partial correlation squared.

[t] p < .10

Table 8

Summary statistics for multiple regression analysis predicting distress during week one and two of the waiting period

Predictors	Beta	Correlation	sr^2(%)	t
Week one				
Age	-.17	-.31	2.4	1.08
Social desirability	-.33	-.40	10.6	2.26*
MBSS-Monitoring	.19	.31	3.0	1.20

Multiple R^2=.25; Adjusted R^2=.19; $F(3, 36)$=4.06, $p < .05$

	Beta	Correlation	sr^2(%)	t
Week two				
Age	-.09	-.27	.0	.54
Years living together	-.21	-.27	4.2	1.48
Social desirability	-.43	-.48	17.5	3.01**
MBSS-Monitoring	.13	.26	1.3	.82

Multiple R^2=.32; Adjusted R^2=.24; $F(4, 35)$=4.13, $p < .05$

Note. sr^2=semi-partial correlation squared.

[t] $p < .10$

* $p < .05$ ** $p < .01$

associated with older age, more years together, less information-seeking and more social desirability. The R^2 value showed that 32% of the variability in distress scores could be accounted for by the set of predictors, with a more substantial unique contribution by social desirability (17.5%).

In summary, the results of these analyses suggest a number of important predictors of distress during IVF-ET. The more important factors in terms of unique contributions to explained variance in distress scores were marital adjustment, childbearing focus, social desirability and information-seeking.

Discussion

I. Emotional reactions during IVF-ET

The most intriguing finding of this study was that women who did not become pregnant with IVF-ET reported experiencing more distress during treatment than those who became pregnant. It will be recalled that the distress subscale of the daily monitoring form assessed the extent to which women experienced a variety of negative affective reactions such as nervousness, infertility stress and pessimism. This group difference on distress cannot be attributed to pre-treatment differences on the demographic, medical or psychological and interpersonal variables assessed in this study because such differences were not obtained. Moreover, analyses carried out with women who had completed a no-treatment month of monitoring showed that the Non-pregnant and Pregnant group were comparable in terms of their emotional, physical and behavioral reactions during this baseline cycle. Thus, group differences on distress during treatment would seem to be attributable to some aspect of the IVF-ET cycle.

In addition to group the differences on distress the Non-pregnant group was also found to have a poorer biological response to IVF-ET, in terms of estradiol levels, oocytes retrieved and embryos transferred to the uterus. These biological variables were found to be significantly correlated to distress during treatment. The direction of causality between distress, biological factors and IVF-ET outcome cannot be inferred on the basis of the design of this study. However, a number of links can be hypothesized.

One possibility for these findings would be that distress reduces the chances of conception. Since the neuroendocrine and/or physiological pathways that could mediate such an effect were not assessed in this study, possible pathways must remain speculative. However, because follicular maturation and ovulation are hormonally controlled in IVF-ET, it would seem unlikely that distress would delay or prevent ovulation, as has been suggested for the impact of psychological factors in donor insemination (Foldes, 1975; Schover et al., 1994). Another pathway suggested by the literature would be that distress increases cortisol which, in turn, interferes with embryonic development such that the success of implantation is compromised. Demyttenaere et al. (1991) found that compared to baseline levels, anxiety, prolactin and cortisol were elevated prior to oocyte retrieval. Michael et al. (1993) found that oocyte exposure to cortisol, as measured by 11beta-HSD activity, did not affect fertilization but reduced implantation rate, suggesting that cortisol may have affected the quality of embryos. Some support for this possibility was provided in this study by the finding that the quality of embryos transferred to the uterus was poorer in the Non-pregnant group as compared to the Pregnant group. A more thorough understanding of the psychoneuroendocrinology of IVF-ET would be required to determine

the specific pathways that could mediate the effects of distress on the success or failure of this intervention.

An alternative hypothesis for the link between distress, biological factors and IVF-ET outcome would be that group differences on distress were due to the greater negative feedback women in the Non-pregnant group likely received about the progress of their IVF-ET trial. While the nature of the feedback patients received was not directly measured in this study, the daily monitoring indicated that the groups differed on distress only during those stages when biological indicators of the progress of IVF-ET were available to medical staff. That is, group differences on distress began to emerge only after the introduction of blood tests to calibrate hMG dosage and ultrasounds to monitor maturing follicles. Group differences were consistently observed from this point until embryo transfer. Discussion with doctors and nursing staff confirmed that feedback about the progress of IVF-ET was routinely provided to patients on the basis of estradiol levels, number of maturing follicles, readiness for hCG, number of oocytes and embryos created or transferred. When biological data were not available to medical staff, that is, during GnRH-a administration, the first five days of hMG administration and the two week waiting period after transfer, group differences on distress were not observed. Because the Non-pregnant group responded more poorly in terms of these biological indicators, they may have received more negative feedback which, in turn, may have lead to the greater distress reported by this group.

The hypothesized link between feedback and distress would be consistent with clinical observations that IVF-ET patients appear to be "exquisitely sensitive" to comments made by medical staff about the progress of IVF-ET and appear to be hypervigilant for any signs that treatment may not

be successful (Seibel & Levin, 1987). Seibel and Levin (1987) have described how patients ask a multitude of questions during ultrasound scanning of maturing follicles and are preoccupied with the number of oocytes or embryos produced. In the present study, a number of women made unsolicited comments on the DRK about the specific estradiol levels reached during ovarian stimulation or the number of oocytes retrieved and embryos transferred. These qualitative findings suggest that women are indeed attentive to comments made by medical staff and therefore potentially vulnerable to the effects of such information on their emotional experience during treatment. However, because the hypothesized link between distress and negative feedback was not directly tested in this study, its validity needs to be confirmed by using an experimental design in which degree and type of information provided to patients and their interpretation of it can be evaluated.

Given the potential for bi-directional links between distress and IVF-ET outcome it may be useful to rely on a biopsychosocial conceptual understanding of causality in this area of study (Engels, 1977; Weiner & Fawzy, 1989). This model has been adopted in diverse areas of health such as coronary heart disease (Endicott, 1989), gastrointestinal disorders (Strang, 1989) and bronchial asthma (Knapp, 1989). In this model, disease is thought to emerge from the complex interplay of biological, psychological and environmental factors. Adopting such a multi-causal model would emphasize the importance of a holistic approach to the understanding of treatment outcome rather than focusing on any one specific link. The research implication of using such a model would be that the additive or interactive effects of each factor (psychological, medical, social) to IVF-ET success would be examined as well as individual contributions. Similarly, the

care of the IVF-ET patient would extend beyond the medical aspects of treatment to include patients' psychological and social needs.

II. Physical and behavioral reactions during IVF-ET

Most of the significant physical and behavioral reactions observed during IVF-ET were due to the demands of the particular stage women were currently involved with. Fatigue was greatest during the stages of ovarian stimulation, ovulation induction and oocyte retrieval. During these stages women attended the clinic on a daily basis to take blood tests, undergo ultrasounds, receive their hMG or hCG injections and undergo the surgical procedures for retrieval. Fatigue was lower during stages where the practical demands of treatment were lower (gonadal suppression, waiting period and pregnancy test).

The pattern of increase in estrogen-related symptoms during the initial stages of IVF-ET was consistent with the rise in estradiol levels. This variable reflected the common side-effects of hMG administration used to induce the estradiol rise: breast tenderness, ovarian pain, abdominal discomfort and bloating. The findings are consistent with those of Leiblum et al. (1987) who found that breast tenderness and abdominal discomfort were greatest during oocyte retrieval when estrogen levels reached their peaks. Interestingly, the Pregnant group did not report more severe estrogen-related symptoms despite the fact they reached, overall, higher estradiol levels than the Non-pregnant group. It may be that differential symptom severity only occurs outside of the range of estradiol levels observed in subjects in this study. Recall that the subject who had the most extreme estradiol levels, that is the subject with the ovarian hyperstimulation syndrome, was not included in the final set of analyses. The only change in physical reactions noted during

embryo transfer and the waiting period was the occurrence of constipation which was likely due to the start of progesterone supplements.

There were few differences between the Non-pregnant and Pregnant groups in terms of physical symptoms and these occurred primarily during the stages of ovarian stimulation and pregnancy test. During ovarian stimulation, the Non-pregnant group reported more dizziness and headaches than the Pregnant group. These are infrequent but potential adverse effects of hMG administration (CPA, 1994). The greater severity of these symptoms in the Non-pregnant group may potentially be related to women's poorer responsiveness to the hMG. In response to the pregnancy test the Non-pregnant group reported a decrease in appetite and more headaches. A decrease in appetite would be consistent with the greater distress observed in this group and may have lead to the greater number of headaches reported. Finally, throughout the treatment cycle the Non-pregnant group reported more fatigue. It is possible that the latter group had more difficulty managing the various practical demands of treatment or that fatigue was a reaction to their poorer biological progress during IVF-ET.

Changes in behavioral symptoms were also stage dependent. Optimism, affection with partner and feelings of pregnancy were generally higher during oocyte retrieval and embryo transfer. Others have also commented on the positive effects of successful embryo transfer (Leiblum et al., 1987; Seibel & Levin, 1987). Because most couples in this study (60%) had never achieved a pregnancy with their partner, successful embryo transfer may also have increased feelings of optimism and closeness because it provided couples with the additional knowledge that they were biologically compatible.

As would be expected, a negative pregnancy test was accompanied by feelings of distress, anxiety and hopelessness. The severity of distress in response to a negative pregnancy test, relative to other stages, confirms that what is hardest about IVF-ET is not the medical procedures per se but its failure. These findings corroborate those of previous studies which found that unsuccessful IVF-ET was associated with an acute period of depression (Hynes et al., 1992; Leiblum et al., 1987; Litt et al., 1992) or anxiety-related symptoms (Newton et al., 1990). However, whether the outcome of IVF-ET was positive or negative, women coped with the results of the pregnancy test through affection and discussion with their spouse, as has been found in previous work (Callan & Hennessey, 1988).

Overall, the consistency between expected changes and reported changes in physical and behavioral reactions serve to provide further validation of the Daily Record Keeping form developed by Takefman et al. (1992). Sensitivity to the changes in these reactions also increases confidence in the reliability of differences obtained between the Non-pregnant and Pregnant women on emotional reactions. Prolonged monitoring raises the question of whether monitoring itself leads to greater reactivity. Although this issue was not addressed in this study, it can be assumed that because the Non-pregnant and Pregnant groups followed the same experimental procedure that such reactivity was inherently controlled for. Moreover, the percentage of subjects with prior monitoring experience, that is, those completing the no-treatment month of monitoring prior to IVF-ET, was equal in the two groups. The major disadvantage of using daily monitoring in research has been the general assumption that patients would refuse to participate because of the time-consuming nature of this methodology. However, in this study it was found that few subjects withdrew from the

study because of this drawback (13% (n=6)). In addition, most subjects reported that the DRK was, overall, neither difficult nor stressful to complete. Together these findings suggest that daily monitoring can usefully capture changes in a variety of reactions during IVF-ET and that it would be a useful tool for both researchers and clinicians working with these patients.

One way in which the findings with the DRK could be used practically would be to better prepare women for some of the reactions they are likely to experience over the course of IVF-ET. Although patients in this study were well-informed of the procedures involved in IVF-ET they felt in greater need of information about the potential risks, such as the side-effects of the medication used. The medical team might consider providing patients with a list of the most commonly reported physical and behavioral reactions at each stage of IVF-ET to help women anticipate the effects of these stages. A number of studies have found that such preparatory information can reduce distress during medical procedures by providing patients with accurate expectations and thereby reducing the unpredictable nature of the upcoming procedure (Ludwick-Rosenthal & Neufeld, 1988).

Another practical use of the DRK would be to identify early in the 45 day course of IVF-ET, patients who are having difficulty managing the demands of treatment. Given the potential influence of distress on IVF-ET outcome, patients experiencing severe psychological distress could be provided with counselling to help them manage more effectively the upcoming demands of the remaining stages of treatment. Future research with the DRK could be aimed at developing normative levels of responding on the basis of which patients responding poorly could be identified.

III. Recall of emotional reactions during treatment

Another important finding in this study was that patients recalled their emotional reactions during treatment differently than when they were experiencing them. Specifically, the daily monitoring form showed that the waiting period was associated with low distress whereas it was recalled as being one of the most stressful stages in the questionnaire completed once women were aware of the results of treatment. The retrospective ratings were consistent with previous retrospective studies that found that the two week waiting period and the beginning of menstruation were recalled as having been the most stressful (Baram et al., 1988; Callan & Hennessey, 1988; Connolly et al., 1993; Leiblum et al., 1987). The discrepancy between prospective and retrospective ratings does not appear to be due to a negative emotional state at the time of recall as would be predicted from previous work (Williams, 1991) because those who were successful with IVF-ET and consequently experiencing little distress showed the same bias as those unsuccessful with it.

Several explanations can be offered to account for the discrepancy between these two sources of information. First, it is possible that the daily distress measure did not reflect well women's concept of stress. On the DRK women rated a variety of negative affective reactions whereas on the retrospective questionnaire they were asked to rate the "stress" of the various stages. However, the finding that prospective and retrospective ratings did not differ for other stages of IVF-ET (ovarian stimulation, oocyte retrieval-embryo transfer, pregnancy test) would argue against this explanation.

Second, it is possible that the discrepancy found between retrospective and prospective accounts reflected women's attempts to cope with the waiting period. Correlations between social desirability and distress at each stage of the IVF-ET process showed that women underreported or suppressed their

treatment distress only during the two week waiting period. A similar reduction in distress was rep rted when women were waiting for the results of natural attempts to conceive during the no-treatment menstrual cycle of monitoring. Social desirability was also found to be related to distress during the luteal phase (r(23)=-.27, p < .10) of that month of monitoring. Women may therefore suppress or downplay their distress as a way of coping with the stressfulness of waiting to find out whether they will become pregnant whether in treatment or not. Callan and Hennessey (1988) found that positive thinking was the most common coping strategy used during IVF-ET. Recall that self-deceptive positivity is one dimension assessed by the social desirability scale used in this study. Because the distress scale of the monitoring form lists only negative affect items, women may have denied any of these reactions because it would have interfered with the use of positivity as a coping strategy. After knowing the outcome of treatment however, when women no longer needed to contain their distress, they may have been able to express their distress more freely in the retrospective questionnaire.

The findings with regard to prospective and retrospective accounts are important in light of the fact that most findings with regard to distress experienced during IVF-ET have been based on retrospective reports (Baram et al., 1988; Callan & Hennessey, 1988; Connolly et al., 1993; Leiblum et al., 1987). On the basis of such findings, it has been concluded that IVF-ET, particularly waiting to find out the results and discovering that it has failed, is moderately to extremely stressful. In contrast, data obtained from the daily monitoring form used in this study would suggest that the waiting period is less distressing and that the initial stages of treatment are more emotionally demanding for women. These discrepancies highlight the importance of

taking into account the measurement format used when interpreting the
results of psychological studies on IVF-ET. This would be particularly
important when findings are used to determine at which stage of treatment
women would be in greatest need of additional support (Connolly et al., 1993).

IV. Predictors of treatment distress

The results of this study suggest some similarities and some differences
between the factors that predict emotional responses to IVF-ET failure and
those that predict emotional reactions to the various stages during treatment.
In this study pre-treatment distress was not found to be related to emotional
reactions during treatment. This finding is inconsistent with predictive
studies that found that anxiety or depression prior to IVF-ET were related to
anxiety or depression once treatment had failed (Newton et al., 1990; Litt et al.,
1992). This inconsistency may be explained by measurement differences
between this study and previous ones. In the current study, different
inventories were used to assess distress prior to IVF-ET (anxiety, several
measures of infertility distress) and during treatment (daily monitoring),
whereas in previous studies the same inventory was used. The relationship
between distress at the two time points reported in past studies may therefore
have been due, in part, to method variance or test-retest reliability. In
support of this explanation, STAI-state scores obtained prior to IVF-ET were
found to be unrelated to distress when treatment failed, as reported on the
DRK, but significantly related to STAI-state scores obtained at that time
$(r(40)=.38, p < .05)$.

One consistent finding between the predictive studies and the current
one was the importance of childbearing focus to feelings of distress during
treatment. Previous studies have found that women who place greater

importance on having a child, as measured by a variety of factors, experience more distress about their infertility (Abbey et al., 1992; McEwan et al., 1987) and expect more stress during treatment (Collins et al., 1992). Predictive studies have found that childless women are at greater risk for poorer adjustment to IVF-ET failure (Newton et al., 1990; Leiblum et al., 1987) and these women have been found to score more highly on childbearing focus (Collins et al., 1992). From a clinical perspective this finding suggests that helping women have a more balanced view of other potential sources of life satisfaction, such as their career or relationships, could ultimately help reduce the distress they experience when in treatment.

It was also found that those who scored relatively lower on marital adjustment or who had been living with their partners for fewer years reported more distress during treatment. Given that the spouse is generally the principal source of support during IVF-ET (Callan & Hennessey, 1988) it would be important to intervene with these couples prior to the start of treatment.

The type of coping strategy women used was also found to be related to their emotional reactions during treatment. Specifically, it was found that women who used information-seeking coping strategies experienced greater treatment distress, particularly during the two week waiting period. Women who rely on monitoring strategies tend to seek out information as a way of coping with stressful events. Since the two week waiting period provides little opportunity to meet this need either through communication with staff or other patients, information-seeking would, by nature, be an ineffective way of coping in this period. This is an important finding in light of the fact that the majority of women in this study relied primarily on information-seeking as a way of coping with stressful situations.

As discussed previously, women were found to underreport or downplay their distress during treatment as shown through correlations with social desirability. Suppression, denial or other ways in which distress can be minimized, as measured by the component of self-deceptive positivity within the social desirability scale, is an important component of emotion-focused types of coping strategies (Lazarus & Folkman, 1984; Aldwin & Revenson, 1987). It is noteworthy that while such strategies were found to be beneficial during treatment, predictive studies have found them to be less effective in managing distress when treatment fails (Hynes et al., 1992; Litt et al., 1992). This differential effectiveness suggests that women must have a diverse repertoire of coping strategies and be flexible in using these to meet the various demands of IVF-ET. Moreover, it suggests that psychological interventions aimed at alleviating the strains of IVF-ET would need to be tailored to the demands of specific stages of this intervention rather than treatment as a whole.

Conclusions and recommendations

The findings of this study raise several methodological, conceptual and clinical points. One major methodological point is that the timing of our assessments (prospective, retrospective) will determine the conclusions we make about emotional reactions to IVF-ET. Patients' recall of treatment distress is not consistent with their ongoing experience of it. Because most of our knowledge about the experience of treatment is based on retrospective ratings we may in fact be making decisions about research and clinical interventions on the basis of a distorted picture of what treatment is like. By utilizing both prospective measures, as well as conventional ones in future

research, it would be possible to differentiate artifacts of memory from valid findings and reduce some of the contradictory findings in this area.

A second methodological point is that multi-item inventories provide a more accurate account of women's experiences during IVF-ET than do single questions about the overall impact of IVF-ET. Analyses of emotional, physical and behavioral reactions clearly demonstrate that the kind and severity of reaction likely to be experienced is determined by the stage of IVF-ET. Because daily recordings of a variety of symptoms can capture more easily the stage or phasic fluctuations in these reactions, using multi-item inventories, like the DRK, would enhance our understanding of the experience of IVF-ET.

The differences obtained on distress between the Non-pregnant and Pregnant group raise a conceptual point about the perceived role of psychological factors in IVF-ET. Although the potential influence of psychological factors in other types of infertility treatments, such as donor insemination, have received some consideration, such attention has been lacking for IVF-ET. It has generally been assumed that the medical and hormonal controls used in this intervention would override any effect that psychological factors could have on the success of treatment. However, the results of this prospective study clearly demonstrate, for the first time, reliable differences in emotional reactions between those who eventually achieve a pregnancy with IVF-ET and those who do not. Although the direction of causality between distress and biological factors could not be established in this study, the results do suggest that research on the relationship between these variables would be worth pursuing.

A number of clinical recommendations can be made on the basis of the results of this study. Given the stage-like nature of IVF-ET, clinicians need to

develop interventions addressed to the specific demands of each stage of this process rather than general interventions. For example, identify ways in which women could better organize their time during the initial stages of treatment so that they are not as tired or provide training in relaxation to reduce distress during the two week waiting period. The demands of each stage could be identified as well as useful coping strategies and these could be provided to patients before they begin treatment.

A second recommendation is that clinicians use the psychological interview typically conducted prior to IVF-ET to identify patients at greater risk for distress during treatment. In this study, women who were very focused on childbearing, who had less stable marriages and who relied on problem-focused as opposed to emotion-focused coping strategies experienced more distress during treatment. Women at risk to experience greater distress during treatment could be monitored more carefully and provided with support when necessary.

In conclusion, the findings of this study indicate that IVF-ET is a demanding treatment for women and is accompanied by a variety of emotional, physical and behavioral reactions. Mental health professionals, as integral participants of the IVF-ET team, can help minimize the strains of treatment by encouraging the team to use of a holistic approach to treatment, one that is attentive to the medical aspects of treatment as well as couples psychological and emotional needs.

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Appendix A: Materials used for Phase I of the study

Interview

Questionnaires: Marital adjustment scale (MAS)

State-trait anxiety inventory (STAI)

Miller Behavioral style scale (MBSS)

Social desirability scale (SDS)

Infertility Questionnaire (IFQ)

Pre-Interview

Name_____   Date_____

Code number: _____

Address: _____

Phone:_____

Referral: _____

I. <u>Background   Information:</u>

1) How old are you?_____

2) What is your occupation?_____

3) What is the last grade (or degree) you attained at school?_____

4) How long have you been living with your current partner? (in
   yrs)_____

5. a) Do you have any children? NO [ ]   YES [ ]   (specify   number)_____

   b) Does your husband have any children? NO [ ]   YES [ ] (specify num) _____

6) If yes, specify for each child his/her <u>year of birth, sex,</u> and whether he/she
   was conceived:
   1-NATURALLY (no medical intervention)
   2-WITH MEDICAL INTERVENTION
   3-ADOPTED

   FIRST CHILD   SECOND CHILD   THIRD CHILD

   sex_____   sex_____   sex_____
   year_____   year_____   year_____
   conceived_____   conceived_____   conceived_____

7) Have you ever sought professional counselling/therapy for any
psychological problems? NO [ ]   Yes [ ]
   If YES, describe the nature of the problem:

   _____

   _____

   _____

8) Do you have any medical problems? (e.g., diabetes, hypertension, asthma, etc.). Any that might interfere with conception? If yes for either question, then; what, duration and how was it treated?

_____

_____

_____

II. <u>Infertility History:</u>

1) How long have you been trying to conceive? Specify in yrs_____

2) Indicate your infertility diagnosis:
   normal or unexplained   [ ]
   endocrine or hormonal factor   [ ]
   tubal   [ ]
   male factor   [ ]
   cervical factor   [ ]
   endometriosis   [ ]
   other_____

3) Did you ever have a
   miscarriage [ ]   ectopic pregnancy [ ]   abortion [ ]

4) How long have you been receiving treatment for your infertility?_____

5) Please indicate in CHRONOLOGICAL order what TREATMENTS you tried <u>before</u> or will try before starting in vitro fertilization (e.g., fertility drugs, surgery).

   <u>TREATMENTS</u>

   a._____ ____

   b._____

   c._____

   d._____

   e._____

6) For each scale below, indicate the answer that best describes the effect INFERTILITY has had on the following aspects of your life.

(a) Relationship issues:

- effect on couple communication:

extremely_____somewhat_____no_____somewhat_____extremely
negative   negative   effect   positive   positive

-effect on marital commitment

extremely_____somewhat_____no_____somewhat_____extremely
negative   negative   effect   positive   positive

(b) Sexual Relationship:

- effect on quality of sexual relationship

extremely_____somewhat_____no_____somewhat_____extremely
negative   negative   effect   positive   positive

(c) Social System:

- effect on social life and friendships

extremely_____somewhat_____no_____somewhat_____extremely
negative   negative   effect   positive   positive

(d) Self-Image:

- effect on the way you see and value yourself (self-esteem)

extremely_____somewhat_____no_____somewhat_____extremely
negative   negative   effect   positive   positive

7) Overall, how well do you feel you have been coping with the strains of infertility?

1_____2_____3_____4_____5
not very well   very well

III. IVF

1) Is this your first attempt at in vitro fertilization?_____

If no, how many times have you tried it and when was your last attempt?

Number of trials _____

Date of last trial _____

Were any of these trials successful?_____

(If trials unsuccessful, specify when failure occurred)

2) Has your doctor (or medical personnel) adequately described the in vitro fertilization procedure to you?

1_____2_____3_____4_____5
not very well   very well

3) Has your doctor (or medical personnel) adequately discussed the possible side effects of treatment?

1_____2_____3_____4_____5
not very well   very well

4)   Are you nervous about undertaking in vitro fertilization?

a) 1_____2_____3_____4_____5
not at all   extremely
nervous/anxious   nervous/anxious

Are you excited (enthusiastic) about trying this procedure?

b) 1_____2_____3_____4_____5
not at all   extremely
enthusiastic   enthusiastic

5a) Rate how disappointed you will be if in vitro fertilization is not successful?

1_____2_____3_____4_____5
not at all   extremely
disappointed   disappointed

5b) Rate how depressed you will be if in vitro fertilization is not successful?

1_____2_____3_____4_____5
not at all   extremely
depressed   depressed

6a) Did your doctor tell you what the success rate (chance of pregnancy) was with in vitro fertilization?   NO [ ]   YES [ ]

IF YES, please indicate the percentage you were told?

0.......10.......20.......30.......40.......50.......60.......70.......80.......90.......100

6b) What do you feel your chances of conceiving are? (express in percentage)?

0....,..10.......20.......30.......40.......50.......60.......70.......80.......90.......100

7) Day of cycle today_____

8) Average length of cycle_____

9) Date will begin monitoring _____ _____

10) Can you be reached at work?_____

Additional comments

_____

_____

_____

_____

_____

_____

_____

Locke-Wallace Marital Adjustment Scale

Please reply to each of the questions by circling the appropriate answer. If you cannot give an exact answer to a question, answer the best you can.

1. Have you ever wished you had not married?
   a. Frequently
   b. Occasionally
   c. Rarely

2. If you had your life to live again, would you:
   a. Marry the same person
   b. Marry a different person
   c. Not marry at all

3. How many outside activities do husband and wife engage in together?
   a. All of them
   b. Some of them
   c. Few of them
   d. None of them

4. In leisure time, which situation do you prefer?
   a. Both husband/wife to stay home
   b. Both to be on the go
   c. One to be on the go and the other to stay home

5. Do you and your mate talk things over together?
   a. Never
   b. Now and then
   ⌐ Almost always
   d. Always

6. How often do you kiss your mate?
   a. Every day
   b. Now and then
   c. Almost never

7. Check any of the following items which you think have caused serious difficulties in your marriage.

- Mate's attempt to control my finances

- Religious differences
     - Different amusement interests
     - Lack of mutual friends
     - Constant bickering
     - Interference of in-laws
     - Lack of mutual affection
     - Unsatisfying sex relations
     - Selfishness/lack of cooperation
- Adultery
     - Desire to have children
     - Infertility husband or wife
     - Venereal diseases
     - Mate became familiar with other
     - Desertion
     - Nonsupport
     - Drunkenness
- Gambling
     - Ill health
     - Mate sent to jail
     - Other reasons

8. How many things truly satisfy you about your marriage?
   a. Nothing   b. One thing
   c. Two things   d. Three or more

9. When disagreement arise, they result in:
   a. Husband giving in
   b. Wife giving in
   c. Neither giving in
   d. Agreement by mutual give and take

10. What is the total number of times you left mate or mate left you due to conflict
    a. No time   b. One or more times

11. How frequently do you or your mate get on each other's nerves around the house?
    a. Never   d. Almost always
    b. Occasionally   e. Always
    c. Frequently

12. What are your feelings on sex relations between you and your mate?
    a. Very enjoyable   c. Tolerable
    b. Enjoyable   d. Disgusting

13. What are your mate's feelings on sex relations with you?
    a. Very enjoyable   c. Tolerable
    b. Enjoyable   d. Disgusting

Indicate approximate extent of agreement between husband and wife

Check one column for each item below*	Always agree	Almost always agree	Occasionally disagree	Frequently disagree	Almost always disagree	Always disagree
	1	2	3	4	5	6
14. Handling family finances						
15. Matters of recreation (eg. going to dance)						
16. Demonstration of affection (eg. kissing frequency)						
17. Friends (eg. dislike of mate's friends)						
18. Intimate relations						
19. Ways of dealing with in-laws						
20. Amount of time that should be spent together						
21. Conventionality (eg. right, good or proper conduct)						
22. Aims, goals and things believed to be important						

23. Circle the dot which you feel best represents the degree of happiness in your marriage

● ● ● ● ● ● ●

very unhappy   very happy

Developed by C. D. Spielberger, R. L. Gorsuch and R. Lushene

STAI FORM X-1

NAME _____ DATE _____

DIRECTIONS: A number of statements which people have used to describe themselves are given below. Read each statement and then blacken in the appropriate circle to the right of the statement to indicate how you *feel* right now, that is, *at this moment.* There are no right or wrong answers. Do not spend too much time on any one statement but give the answer which seems to describe your present feelings best.

	NOT AT ALL	SOMEWHAT	MODERATELY SO	VERY MUCH SO
1. I feel calm	①	②	③	④
2. I feel secure	①	②	③	④
3. I am tense	①	②	③	④
4. I am regretful	①	②	③	④
5. I feel at ease	①	②	③	④
6. I feel upset	①	②	③	④
7. I am presently worrying over possible misfortunes	①	②	③	④
8. I feel rested	①	②	③	④
9. I feel anxious	①	②	③	④
10. I feel comfortable	①	②	③	④
11. I feel self-confident	①	②	③	④
12. I feel nervous	①	②	③	④
13. I am jittery	①	②	③	④
14. I feel "high strung"	①	②	③	④
15. I am relaxed	①	②	③	④
16. I feel content	①	②	③	④
17. I am worried	①	②	③	④
18. I feel over-excited and "rattled"	①	②	③	④
19. I feel joyful	①	②	③	④
20. I feel pleasant	①	②	③	④

SELF-EVALUATION QUESTIONNAIRE
STAI FORM X-2

NAME _____ DATE _____

DIRECTIONS: A number of statements which people have used to describe themselves are given below. Read each statement and then blacken in the appropriate circle to the right of the statement to indicate how you *generally* feel. There are no right or wrong answers. Do not spend too much time on any one statement but give the answer which seems to describe how you *generally* feel.

	ALMOST NEVER	SOMETIMES	OFTEN	ALMOST ALWAYS
21. I feel pleasant	①	②	③	④
22. I tire quickly	①	②	③	④
23. I feel like crying	①	②	③	④
24. I wish I could be as happy as others seem to be	①	②	③	④
25. I am losing out on things because I can't make up my mind soon enough	①	②	③	④
26. I feel rested	①	②	③	④
27. I am "calm, cool, and collected"	①	②	③	④
28. I feel that difficulties are piling up so that I cannot overcome them	①	②	③	④
29. I worry too much over something that really doesn't matter	①	②	③	④
30. I am happy	①	②	③	④
31. I am inclined to take things hard	①	②	③	④
32. I lack self-confidence	①	②	③	④
33. I feel secure	①	②	③	④
34. I try to avoid facing a crisis or difficulty	①	②	③	④
35. I feel blue	①	②	③	④
36. I am content	①	②	③	④
37. Some unimportant thought runs through my mind and bothers me	①	②	③	④
38. I take disappointments so keenly that I can't put them out of my mind	①	②	③	④
39. I am a steady person	①	②	③	④
40. I get in a state of tension or turmoil as I think over my recent concerns and interests	①	②	③	④

Miller Behavioral Style Scale

1. Vividly imagine that you are afraid of the dentist and have to get some dental work done. Which of the following would you do? Check all of the statements that might apply to you.

_____ I would ask the dentist exactly what he was going to do.

_____ I would take a tranquilizer or have a drink before going.

_____ I would try to think about pleasant memories.

_____ I would want the dentist to tell me when I would feel pain.

_____ I would try to sleep.

_____ I would watch all the dentist's movements and listen for the sound of the drill.

_____ I would watch the flow of water from my mouth to see if it contained blood.

_____ I would do mental puzzles in my mind.

2. Vividly imagine that you are being held hostage by a group of armed terrorists in a public building. Which of the following would you do? Check all of the statements that might apply to you.

_____ I would sit by myself and have as many daydreams and fantasies as I could.

_____ I would stay alert and try to keep myself from falling asleep.

_____ I would exchange life stories with the other hostages.

_____ If there was a radio present, I would stay near it and listen to bulletins about what the police were doing.

_____ I would watch every movement of my captors and keep an eye on their weapons.

_____ I would try to sleep as much as possible.

_____ I would think about how nice it's going to be when I get home.

_____ I would make sure I knew where every possible exit was.

3. Vividly imagine that, due to a large drop in sales, it is rumored that several people in your department at work will be laid off. Your supervisor has turned in an evaluation of your work for the past year. The decision about lay-offs has been made and will be announced in several days. Check all the statements that might apply to you.

_____. I would talk to my fellow workers to see if they knew anything about what the supervisor's evaluation of me said.

_____ I would review the list of duties for my present job and try to figure out if I had fulfilled them all.

_____ I would go to the movies to take my mind off things.

_____ I would try to remember any arguments or disagreements I might have had with the supervisor that would have lowered his opinion of me.

_____ I would push all thoughts of being laid off out of my mind.

_____ I would tell my spouse that I'd rather not discuss my chances of being laid off.

_____ I would try to think which employees in my department the supervisor might have thought had done the worst job.

_____ I would continue doing my work as if nothing special was happening.

4. Vividly imagine that you are on an airplane, thirty minutes from your destination, when the plane unexpectedly goes into a deep dive and then suddenly levels off. After a short time, the pilot announces that nothing is wrong, although the rest of the ride may be rough. You, however, are not convinced that all is well. Check all the statements that might apply to you.

_____ I would carefully read the information provided about safety features in the plane and make sure I knew where the emergency exits were.

_____ I would make small talk with the passenger beside me.

_____ I would watch the end of the movie, even if I had seen it before.

_____ I would call for the stewardess and ask her exactly what the problem was.

_____ I would order a drink or tranquilizer from the stewardess.

_____ I would listen carefully to the engine for unusual noises and would watch the crew to see if their behaviour was out of ordinary.

_____ I would talk to the passenger beside me about what might be wrong.

_____ I would settle down and read a book or magazine or write a letter.

Name _____   Date _____

Social Desirability Scale

Listed below are a number of statements concerning attitudes and traits. Read each item and decide whether the statement is true or false as it pertains to you personally. Please indicate your response by circling true ("T") or false ("F").

1. Before voting I thoroughly investigate the qualifications of all candidates.   T   F

2. I never hesitate to go out of my way to help someone in trouble.   T   F

3. It is sometimes hard for me to go on with my work if I am not encouraged.   T   F

4. I have never intensely disliked anyone.   T   F

5. On occasion I have had doubts about my ability to succeed in life.   T   F

6. I sometimes feel resentful when I don't get my way.   T   F

7. I am always careful about my manner of dress.   T   F

8. My table manners at home are as good as when I eat out in a restaurant.   T   F

9. If I could get into a movie without paying and be sure I was not seen I would probably do it.   T   F

10. On a few occasions, I have given up doing something because I thought too little of my ability.   T   F

11. I like to gossip at times.   T   F

12. There have been times when I felt like rebelling against people in authority even though I knew they were right.   T   F

13. No matter who I'm talking to, I'm always a good listener.   T   F

14. I can remember "playing sick" to get out of something.   T   F

15. There have been occasions when I took advantage of someone.   T   F

16. I'm always willing to admit it when I make a mistake.   T   F

17. I always try to practice what I preach.   T   F

18. I don't find it particularly difficult to get along
with loud mouthed, obnoxious people.   T   F

19. I sometimes try to get even rather than forgive and forget.   T   F

20. When I don't know something I don't at all mind admitting it.   T   F

21. I am always courteous, even to people who are disagreeable.   T   F

22. At times, I have really insisted on having things my own way.   T   F

23. There have been occasions when I felt like smashing things.   T   F

24. I would never think of letting someone else be punished
for my wrongdoing.   T   F

25. I never resent being asked to return a favour.   T   F

26. I have never been irked when people expressed ideas
very different from my own.   T   F

27. I never make a long trip without checking the safety
of my car.   T   F

28. There have been times wnen I was quite jealous of
the good fortune of others.   T   F

29. I have almost never felt the urge to tell someone off.   T   F

30. I am sometimes irritated by people who ask favors of me.   T   F

31. I have never felt that I was punished without cause.   T   F

32. I sometimes think when people have a misfortune they
only got what they deserved.   T   F

33. ᵀ have never deliberately said something that hurt
someone's feelings.   T   F

Infertility Questionnaire

INSTRUCTIONS: Please circle the number closest to the reactions that most accurately expresses your current feelings.

REPONSES				
Strongly Agree	Agree	Neutral	Diasgree	Strongly Disagree
5	4	3	2	1

1. I feel bad about my body because of our inability to have a child.

5	4	3	2	1

2. Since our infertility I feel I can do anything as well as I used to.

5	4	3	2	1

3. I feel I am as attractive as before our infertility.

5	4	3	2	1

4. I feel less feminine because of our inability to have a child.

5	4	3	2	1

5. Compared to others, I feel I am a worthwhile person.

5	4	3	2	1

6. Lately, I feel I am sexually attractive to my partner.

5	4	3	2	1

7. I feel I will be incomplete as a woman if we cannot have a child.

5	4	3	2	1

8. Having an infertility problem makes me feel physically incompetent.

5	4	3	2	1

9. I feel guilty about somehow causing our infertility.

5	4	3	2	1

REPONSES				
Strongly Agree	Agree	Neutral	Diasgree	Strongly Disagree
5	4	3	2	1

10. I wonder if our infertility problem is due to something I did in the past.

| 5 | 4 | 3 | 2 | 1 |

11. My spouse makes me feel guilty about our problem.

| 5 | 4 | 3 | 2 | 1 |

12. There are times when I blame my partner for our infertility.

| 5 | 4 | 3 | 2 | 1 |

13. I feel I am being punished because of our infertility.

| 5 | 4 | 3 | 2 | 1 |

14. Lately, I feel I am able to respond to my spouse sexually.

| 5 | 4 | 3 | 2 | 1 |

15. I feel sex is a duty, not a pleasure.

| 5 | 4 | 3 | 2 | 1 |

16. Since our infertility problem, I enjoy sexual relations with my spouse.

| 5 | 4 | 3 | 2 | 1 |

17. We have sexual relations for the purpose of trying to conceive.

| 5 | 4 | 3 | 2 | 1 |

18. Sometimes I feel like a "sex machine" programmed to have sex during the fertile period.

| 5 | 4 | 3 | 2 | 1 |

19. Impaired fertility has helped our sexual relationship.

| 5 | 4 | 3 | 2 | 1 |

20. Our inability to have a child has increased my desire for sexual relations.

| 5 | 4 | 3 | 2 | 1 |

REPONSES				
Strongly Agree	Agree	Neutral	Diasgree	Strongly Disagree
5	4	3	2	1

21. Our inability to have a child has <u>decreased</u> my desire for sexual relations.

5	4	3	2	1

22. I will do anything to have a child.

5	4	3	2	1

23. I think often of our infertility.

5	4	3	2	1

24. Having a child is the major focus of my life.

5	4	3	2	1

25. Infertility is one of the hardest problems of my life.

5	4	3	2	1

Appendix B: Materials used for Phase II of the study

Daily Record Keeping Sheet (DRK)

Retrospective questionnaire

Daily Record Keeping Sheet
Takelman & Boivin, 1990.

Day of Cycle								
Date								
Intercourse								
Treatment								
Section I								
Nervousness								
Moodiness								
Irritability								
Sadness								
Touchy/Sensitive								
Pessimistic								
Unfulfilled								
Anger								
Hassled								
Frustration								
Infertility Stresses								
Dizziness								
Nausea								
Fatigue								
Breast Tenderness								
Abdominal Bloating								
Abdominal Discomfort								
Ovarian Pain								
Constipation								
Weight Gain								
Weight Loss								
Increased Appetite								
Decreased Appetite								
Insomnia								
Headaches								
Section II								
Feeling Pregnant								
Pregnancy Dreams								
Optimistic: Pregnancy								
Sexual Fantasies								
Sexual Desire								
Arguments/Partner								
Affection/Partner								
Good Talk/Partner								
Lack of concentration at work								
Socializing/Friends								

Codes

B = Blood Flow
PI = Pergonal Injections
C = Clomid/Serophene
L = Lupron
U = Ultrasound(s)
OR = Egg Retrieval
ET = Embryo Transfer
AI = Insemination day(s)
P = Progesterone
PT = Pregnancy Test

ANALOG

NONE   MILD   MODERATE   SEVERE

No: _____
Name: _____
Date: _____
Cycle: No-treatment   Treatment
Week: 1 2 3 4 5

INSTRUCTIONS FOR DAILY RECORD KEEPING SHEET

1. Fill in **name, date**, whether this is No-treatment or Treatment cycle of daily monitoring, and whether this is **week** 1, 2, 3, 4, or 5 of your menstrual cycle in the shaded box at the bottom right.

2. **Day of Cycle**: The first day of the menstrual cycle (at the top of the chart) is calculated as the first day of menstrual bleeding.

3. **Date**: Record the dates of the month which correspond with the days of your menstrual cycle.

4. **Intercourse**: On the days you engage in intercourse mark an 'X' in the corresponding boxes.

5. **Treatment**: In the box labelled **Codes** are the names of events occurring in different infertility treatments. Use these codes to indicate on the **Treatment** line the events you have experienced that day. For example, you would insert a 'B' on the days you experience your blood flow, or a 'U' on the days you had an ultrasound. Some of these codes will apply to you and others will not. Be sure to use only those you have experienced.

Section I

A list of various symptoms generally encountered during a menstrual cycle appear in the first section. If there are terms you do not understand please ask the nurse or technician to explain them to you.

On a daily basis you are to fill in the corresponding boxes to indicate to what extent you are experiencing each one of these symptoms. You should fill in the chart at the same time of each day, before you go to sleep, and reflect on the past 24 hours in terms of whether and to what extent the symptom occurred, regardless of whether the symptoms were associated with conception. These symptoms are graded as follows:

NONE   MILD   MODERATE   SEVERE

Legend:
None - the symptom is not present.
Mild - the symptom is present but does not interfere with activities.
Moderate - the symptom is present and interferes to some degree with activities.
Severe - efficiency of performing some daily tasks is markedly reduced.

Section II

A list of different feelings/occurrences are listed in the second section. If there are any words/phrases you do not understand, please ask the nurse/technician for clarification. If you experienced any of these feelings/occurrences on a given day indicate it by putting a tick '   ' in the corresponding box.

NB. These record keeping forms are to be filled out on a daily basis for your entire menstrual cycle, until the third day of the next period. You will be provided with five charts, with each chart corresponding to one week (7 days) of record keeping. At the end of each week mail the record keeping form in the stamped, pre-addressed envelope provided.

Retrospective Questionnaire

Code Number _____   Date _____

INSTRUCTIONS: The following questions ask about your experience with in vitro fertilization-embryo transfer (IVF-ET). Please answer each question to the best of your knowledge. Some questions will apply to you and others will not. If a question does not apply to you simply write 'not applicable' or N/A. Please be sure to answer all questions that apply to you. To maintain your anonymity only your code number is used on this interview.

1) Rate how stressful you found each of the following aspects of the IVF-ET process by circling the number that corresponds best to the stress you experienced.

a) waiting to try IVF
    1_____2_____3_____4_____5
    not at all   extremely
    stressful   stressful

b) ovarian stimulation
(Pergonal, blood tests,
    ultrasounds)
    1_____2_____3_____4_____5
    not at all   extremely
    stressful   stressful

c) stress on husband
    in providing sperm
    (estimate)
    1_____2_____3_____4_____5
    not at all   extremely
    stressful   stressful

d) egg retrieval and embryo
    transfer
    1_____2_____3_____4_____5
    not at all   extremely
    stressful   stressful

e) waiting the 2 weeks
before pregnancy test
    1_____2_____3_____4_____5
    not at all   extremely
    stressful   stressful

f) day of the pregnancy test
    (going and receiving results)
    1_____2_____3_____4_____5
    not at all   extremely
    stressful   stressful

2. Did you become pregnant this month as a result of in vitro fertilization?

    No _____
    Yes _____

3) How many days ago did you find out the results of treatment _____ day(s)

4) How stressful did you fii , completing the Daily Record-Keeping Form?

1_____2_____3_____4_____5
not at all   extremely
stressful   stressful

5) How difficult was it to complete the Daily Record-Keeping Form?

1_____ _2_____3_____4_____5
not at all   extremely
difficult   difficult

Additional comments

_____

_____

_____

_____

_____

Please complete the questionnaire attached to this interview

Appendix C

Consent form

Medical authorization form

Consent Form

Although in vitro fertilization-embryo transfer has been used for the last decade in the treatment of infertility, relatively little is known of the impact of this treatment on women's emotional and physical functioning. The major objective of this study is to gain more understanding of how patients react to this treatment. The information you provide will be invaluable in helping us better meet the psychological and medical needs of couples trying to become pregnant with this method.

Participation in this project would entail completing two (2) interviews (one in person and one written interview), five (5) questionnaires and a daily record-keeping form. The purpose of the interviews is to obtain information about your reproductive history and reactions to the treatment protocol. The questionnaires inquire about other aspects of your life such as your marital relationship and coping style. The interview will be completed with a clinical psychologist while the written interview and questionnaires will be completed at home. A daily record-keeping sheet will be completed over two months; one month prior to beginning an IVF-ET cycle and one month during treatment. The record-keeping form monitors daily fluctuations in physical (e.g., nausea, headaches) and emotional (e.g., moodiness, sensitivity) symptoms. It takes no longer than a few minutes to complete everyday. All information provided by participants will be held in the strictest of confidence. Interviews and questionnaire completion will be conducted privately between the psychologist and participant. The attending physician and the staff at the Institut **will not** have access to your responses without your written permission.

I understand that my participation in this project will involve completing a series of five questionnaires (30 minutes total), one in person interview (1 hour), one written interviews (15 minutes) and a daily record keeping form (5 minutes each day) prior to and during treatment.

I understand that my decision regarding participation in this study will in no way affect the medical management of my condition.

I understand that I am free to ask any questions concerning the procedures used in this project at any time. If for any reasons I experience discomfort or concern during participation in this project, I am free to withdraw, or discuss this with the research psychologist or my physician and request appropriate recommendations or referrals. I understand that withdrawal from the study at any time will not affect the medical management of my condition.

I understand that during my participation in this study I must inform the research psychologist if I seek professional counselling because of my infertility or attend any infertility support groups.

I am informed that upon completion of this study, I am welcome to inquire and receive information pertaining to my individual and the overall results of the study.

I understand that if the results of this study are published, that my part in the study will be completely anonymous and my privacy will be protected.

I _____consent to participate in the study conducted by Jacky Boivin, M.A., C.P.P.Q. under the supervision of William Brender, Ph.D. of the Department of Psychology, Concordia University with the collaboration of the IVF-ET clinic.

Signed:

Date:

I, _____certify that I have explained to the above named patient, the nature of the study and that the patient has the option of withdrawing from the study at any time.

Signed:

Date:

Autorisation de communiquer des renseignements
Authorization to release information

Date: _____

Je, soussigné _____
I, the undersigned

authorise Dr. _____
authorize

à communiquer à _____
to communicate to

des renseignements relier à mon traitement de fécondation in vitro à la clinique de fertilité
information related to my treatment with in vitro fertilization at the fertility clinic

pour la période de _____
for the period of

contenus dans le dossier médical de _____
contained in the medical record of

_____

nom/family name   prénom/given name

_____

adresse/address

_____

signature de la patiente   date
signature of patient

Cette autorisation est valable pour les services médicaux reçus durant les quatre-vingt- dix (90) jours suivant la date de la signature de ce document.

This authorization is valid for the medical services received during the ninety (90) days following the date this document was signed.

Appendix D: Tables for Figures presented in results section

Table 1

<u>Means (SD) for Domain difference score for the combined sample (n=42)</u>

<u>presented in text as Figure 1</u>

Domain [a]	Mean (SD)	$F_{(1, 41)}$ [b]
Communication	.405 (.89)	8.78**
Commitment	.476 (.77)	15.95**
Sexual relationship	-.190 (.71)	3.05[t]
Family and social relationships	-.214 (.61)	5.25*
Self-esteem	-.167 (.66)	2.68

[a] Higher scores indicate more positive effects.

[b] F-ratio compares Domain difference score against constant of zero.

[t] $p \le .01$
[*] $p \le .05$
[**] $p \le .01$

Table 2

Overall and group means (SD) for distress scores as a function of Phase of the no-treatment menstrual cycle for the combined sample (n=20) presented in text as Figure 2

Domain	Overall	Non-pregnant	Pregnant
Follicular	.141(.13)	.141 (.13)	.093 (.10)
Ovulatory	.094 (.08)	.094 (.08)	.035 (.09)
Luteal	.022 (.03)	.022 (.03)	.012 (.02)
Menstrual	.056 (.06)	.056 (.06)	.128 (.25)

Table 3

Means (SD) for fatigue as a function of Phase of the no-treatment menstrual cycle for the combined sample (n=20) presented in text as Figure 3

Phase	Fatigue
Follicular	.517 (.39)
Ovulatory	.267 (.61)
Luteal	.079 (.14)
Menstrual	.546 (.59)

Table 4

Means (SD) for affection and good talk with partner and socializing as a function of Phase of the no-treatment menstrual cycle for the combined sample (n=20) presented in text as Figure 4

	Variable		
	Affection	Good talk	Socializing
Phase			
Follicular	.222 (.16)	.266 (.21)	.212 (.15)
Ovulatory	.467 (.40)	.367 (.39)	.333 (.34)
Luteal	.071 (.09)	.046 (.07)	.100 (.10)
Menstrual	.247 (.37)	.233 (.33)	.297 (.28)

Table 5

Means (SD) for distress scores as a function of Pregnancy group and Stage of
IVF-ET presented in text as Figure 5

| | Group | | |
| | Non-pregnant | Pregnant | |
Stage	(n=23)	(n=17)	F(1, 38)
Hormonal suppression	.133 (.11)	.095 (.09)	1.34
hMG - only	.157 (.13)	.109 (.11)	1.64
hMG - plus	.223 (.23)	.095 (.09)	5.61*
Ovulation induction	.249 (.19)	.117 (.16)	5.56*
Oocyte retrieval	.253 (.19)	.127 (.12)	6.35*
Embryo transfer	.213 (.09)	.099 (.08)	4.04*
Week one	.102 (.09)	.067 (.06)	2.28
Week two	.183 (.16)	.121 (.09)	2.43
Pregnancy test	.856 (.70)	.110 (.09)	25.60***

* p ≤ .05

*** p ≤ .001

Table 6

Means (SD) for estrogen-related symptoms as a function of Stage of IVF-ET for the combined sample (n=40) presented in text as Figure 6

	Estrogen-related symptoms
Stage	
Hormonal suppression	.218 (.23)
Ovarian stimulation	.312 (.27)
Ovulation induction	.552 (.45)
Oocyte retrieval-embryo transfer	.816 (.60)
Waiting period	.563 (.36)
Pregnancy test	.477 (.43)

(Comparison F-values for these means presented in Appendix E.1)

Table 7

Means (SD) for constipation as a function of Stage of IVF-ET for the combined sample (n=40) presented in text as Figure 7

Stage	Constipation
Hormonal suppression	.067 (.13)
Ovarian stimulation	.098 (.16)
Ovulation induction	.102 (.30)
Oocyte retrieval	.150 (.36)
Embryo transfer	.317 (.76)
Waiting period	.256 (.33)
Pregnancy test	.059 (.19)

(Comparison F-values for these means presented in Appendix E.2)

Table 8

Means (SD) for fatigue as a function of Stage of IVF-ET for the combined
sample (n=40) presented in text as Figure 8

Stage	Fatigue
Hormonal suppression	.642 (.53)
Ovarian stimulation	.970 (.66)
Ovulation induction	.877 (.85)
Oocyte retrieval	1.000 (1.18)
Embryo transfer	.366 (.62)
Waiting period	.318 (.35)
Pregnancy test	.499 (.58)

(Comparison F-values for these means presented in Appendix E.3)

Table 9

Means (SD) for dizziness as a function of Pregnancy group and Stage of IVF-
ET presented in text as Figure 9

| | Group | | |
Stage	Not Pregnant (n=23)	Pregnant (n=17)	F (1,38)
Hormonal suppression	.113 (.14)	.061 (.11)	1.82
Ovarian stimulation	.220 (.40)	.067 (.14)	2.96^t
Ovulation induction	.218 (.66)	.063 (.25)	1.10
Oocyte retrieval	.917 (1.28)	.125 (.50)	7.45**
Embryo transfer	.087 (.41)	.067 (.25)	.04
Waiting period	.067 (.10)	.005 (.04)	9.30**
Pregnancy test	.067 (.21)	.023 (.08)	.85

^{t} $p \leq .10$

** $p \leq .01$

Table 10

Means (SD) for headaches as a function of Pregnancy group and Stage of IVF-
ET presented in text as Figure 10

| | Group | | |
| | Not Pregnant | Pregnant | |
Stage	(n=23)	(n=17)	F (1,38)
Hormonal suppression	.358 (.28)	.248 (.29)	1.46
Ovarian stimulation	.398 (.40)	.200 (.20)	4.20*
Ovulation induction	.091 (.29)	.059 (.24)	.14
Oocyte retrieval-embryo transfer	.087 (.25)	.088 (.26)	.00
Waiting period	.156 (.16)	.068 (.11)	4.12*
Pregnancy test	.475 (.52)	.002 (.01)	19.18***

*$p \leq .05$

***$p \leq .001$

Table 11

Overall and group means (SD) for optimism as a function of Pregnancy group and of Stage of IVF-ET presented in text as Figure 11

| | Group | | | |
| | Overall | Not Pregnant | Pregnant | |
Stage	(n=40)	(n=23)	(n=17)	F (1, 38)
Gonadal suppression	.183 (.33)	.242 (.33)	.105 (.14)	3.10^t
Ovarian stimulation	.256 (.29)	.278 (.32)	.225 (.25)	.35
Ovulation induction	.461 (.50)	.454 (.50)	.471 (.51)	.01
Oocyte retrieval-				
Embryo transfer	.450 (.45)	.457 (.42)	.441 (.50)	.01
Waiting period	.262 (.30)	.320 (.30)	.184 (.28)	2.19
Pregnancy test	.101 (.24)	.020 (.07)	.210 (.34)	5.24*

^{t} $p \leq .10$

* $p \leq .05$

(Comparison F-values for overall means presented in Appendix E.4)

Table 12

Means (SD) for affection with partner as a function of Stage of IVF-ET for the
combined sample (n=40) presented in text as Figure 12

Stage	Affection
Hormonal suppression	.363 (.32)
Ovarian stimulation	.356 (.30)
Ovulation induction	.393 (.47)
Oocyte retrieval-embryo transfer	.566 (.43)
Waiting period	.368 (.31)
Pregnancy test	.536 (.40)

(Comparison F-values for these means presented in Appendix E.5)

Table 13

Means (SD) for good talk with partner as a function of Stage of IVF-ET for the combined sample (n=40) presented in text as Figure 13

Stage	Good talk
Hormonal suppression	.290 (.29)
Ovarian stimulation	.320 (.30)
Ovulation induction	.366 (.46)
Oocyte retrieval-embryo transfer	.341 (.38)
Waiting period	.269 (.27)
Pregnancy test	.499 (.39)

(Comparison F-values for these means presented in Appendix E.6)

Table 14

Means (SD) for socializing as a function of Stage of IVF-ET for the combined sample (n=40) presented in text as Figure 14

Stage	Socializing
Hormonal suppression	.313 (.26)
Ovarian stimulation	.307 (.24)
Ovulation induction	.386 (.49)
Oocyte retrieval-embryo transfer	.138 (.28)
Waiting period	.282 (.23)
Pregnancy test	.348 (.33)

(Comparison F-values for these means presented in Appendix E.7)

Table 15

Means (SD) for estradiol level at each successive blood test day as a as a
function of Pregnancy group presented in text as Figure 15

| | Group | | |
Stage	Non-pregnant	Pregnant	F
Day 1	868.09 (538.6)	977.24 (177.6)	.27
Day 2	1532.96 (976.1)	2399.24 (1565.1)	4.04[t]
Day 3	2071.22 (1376.0)	3559.94 (2222.3)	5.95*
Day 4	2992.91 (2213.5)	5355.31 (3492.7)	5.71*
Day 5	3751.13 (2039.5)	6520.77 (4238.6)	4.84*
Day 6	4875.70 (2606.0)	5718.13 (1264.0)	-
Day 7	4503.44 (1857.0)	3206.00 (1324.0)	-
Day 8	2912.00 (1698.5)	3607.00 (2217.5)	-

Note. Sample size in the two groups varied across blood test days because
women differed in the number of days of hMG required to achieve optimal
estradiol level. Because sample size was markedly reduced after Day 6, F-tests
were not computed.

[t] $p < .10$

* $p \leq .05$

Table 16

Means (SD) for standardized stress ratings as a function of Method of measurement and Stage of IVF-ET for the combined sample (n=40) as presented in Figure 16

Stage	Method		
	Prospective	Retrospective	$F(1,38)$
Ovarian stimulation	-.634 (1.03)	-.821 (1.05)	.88
Oocyte retrieval-embryo transfer	-.466 (1.06)	-.452 (1.03)	.00
Waiting period	-1.338 (.99)	.654 (1.05)	90.63***
Pregnancy test	.540 (1.21)	.719 (1.05)	.69

*** $p \leq .001$

Appendix E: Comparison F-values for variables showing

significant main effects of Stage

E.1: Estrogen-related symptoms

E.2: Constipation

E.3: Fatigue

E.4: Optimism

E.5: Affection with partner

E.6: Good talk with partner

E.7: Socializing

Appendix E.1 Comparison F-values for estrogen-related symptoms across stages of IVF-ET

Stages	Means:	1 .218	2 .312	3 .552	4 .816	5 .563	6 .477
1. Hormonal suppression		X					
2. Ovarian stimulation		4.80 (.034)	X				
3. Ovulation induction		29.27 (.000)	21.90 (.000)	X			
4. Oocyte retrieval- Embryo transfer		57.30 (.000)	35.05 (.000)	14.21 (.001)	X		
5. Waiting period		50.55 (.000)	24.30 (.000)	.04 (.851)	12.25 (.001)	X	
6. Pregnancy test		17.39 (.000)	8.12 (.007)	1.42 (.243)	13.99 (.001)	2.82 (.106)	X

Note. F-values presented first; significance values in parentheses. Bold values indicate significant or marginally significant comparsions.

Appendix E.2 Comparison F-values for Constipation across stages of IVF-ET

Stages	Means:	1 .067	2 .098	3 .102	4 .150	5 .317	6 .256	7 .059
1. Hormonal suppression		$\underline{X}$						
2. Ovarian stimulation		2.13 (.153)	$\underline{X}$					
3. Ovulation induction		.86 (.358)	.01 (.910)	$\underline{X}$				
4. Oocyte retrieval		1.81 (.078)	.98 (.338)	.61 (.443)	$\underline{X}$			
5. Embryo transfer		4.92 (.032)	3.96 (.060)	3.88 (.056)	2.85 (.100)	$\underline{X}$		
6. Waiting period		15.21 (.000)	9.36 (.004)	7.62 (.009)	2.82 (.100)	.34 (.565)	$\underline{X}$	
7. Pregnancy test		.05 (.898)	.86 (.361)	.55 (.467)	1.80 (.188)	17.14 (.000)	4.37 (.043)	$\underline{X}$

Appendix E.3 <u>Comparison F-values for fatigue across stages of IVF-ET</u>

Stages	Means:	1 .642	2 .970	3 .877	4 1.00	5 .366	6 .318	7 .499
1. Hormonal suppression	X							
2. Ovarian stimulation		15.37 (.000)	X					
3. Ovulation induction		4.16 (.048)	1.21 (.276)	X				
4. Oocyte retrieval		3.76 (.060)	.029 (.867)	.476 (.496)	X			
5. Embryo transfer		6.00 (.019)	21.53 (.000)	12.04 (.001)	12.46 (.001)	X		
6. Waiting period		17.56 (.000)	41.22 (.000)	20.70 (.000)	15.52 (.000)	.211 (.648)	X	
7. Pregnancy test		1.46 (.234)	12.32 (.001)	6.30 (.016)	6.20 (.017)	1.33 (.258)	4.62 (.038)	X

Appendix E.4 Comparison F-values for optimism across stages of IVF-ET

Stages	1	2	3	4	5	6
Means:	.184	.256	.461	.450	.262	.101
1. Hormonal suppression	$\underline{X}$					
2. Ovarian stimulation	4.97 (.032)	$\underline{X}$				
3. Ovulation induction	13.91 (.001)	10.43 (.003)	$\underline{X}$			
4. Oocyte retrieval/ Embryo transfer	15.68 (.000)	12.74 (.001)	.040 (.845)	$\underline{X}$		
5. Waiting period	2.31 (.136)	.017 (.898)	7.90 (.008)	10.50 (.002)	$\underline{X}$	
6. Pregnancy test	2.25 (.143)	8.12 (.007)	21.34 (.000)	21.34 (.000)	10.11 (.003)	$\underline{X}$

Appendix E.5 Comparison F-values for affection across stages of IVF-ET

Stages	1	2	3	4	5	6
Means:	.363	.356	.393	.566	.368	.536
1. Hormonal suppression	X					
2. Ovarian stimulation	.032 (.858)	X				
3. Ovulation induction	.212 (.650)	.436 (.516)	X			
4. Oocyte retrieval/ Embryo transfer	9.85 (.003)	13.32 (.001)	5.15 (.029)	X		
5. Waiting period	.029 (.868)	.109 (.744)	.160 (.690)	12.60 (.001)	X	
6. Pregnancy test	6.10 (.018)	7.40 (.010)	3.50 (.069)	.152 (.698)	7.56 (.009)	X

Appendix E.6 Comparison F-values for good talk across stages of IVF-ET

Stages	1	2	3	4	5	6
Means:	.290	.320	.366	.341	.269	.499
1. Hormonal suppression	X					
2. Ovarian stimulation	.624 (.434)	X				
3. Ovulation induction	1.51 (.225)	.462 (.498)	X			
4. Oocyte retrieval/ Embryo transfer	1.28 (.265)	.336 (.567)	.144 (.707)	X		
5. Waiting period	.372 (.547)	2.53 (.120)	2.66 (.111)	3.92 (.055)	X	
6. Pregnancy test	12.53 (.001)	9.24 (.004)	3.34 (.074)	7.73 (.008)	18.23 (.000)	X

Appendix E.7 Comparison F-values for socializing across stages of IVF-ET

Stages	1	2	3	4	5	6
Means:	.313	.307	.386	.138	.282	.348
1. Hormonal suppression	X					
2. Ovarian stimulation	.102 (.754)	X				
3. Ovulation induction	.548 (.466)	.810 (.374)	X			
4. Oocyte retrieval/ Embryo transfer	21.16 (.000)	17.14 (.001)	8.58 (.006)	X		
5. Waiting period	.281 (.597)	.044 (.833)	1.02 (.320)	17.22 (.000)	X	
6. Pregnancy test	1.64 (.209)	2.04 (.162)	.078 (.781)	17.06 (.000)	2.69 (.110)	X