

How to treat depression, stress associated with infertility Tx

Your understanding can ease the emotional roller coaster

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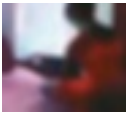
“ I think it's my fault we can't get pregnant,” says Mrs. S, who has been referred by her gynecologist for evaluation of anxiety and depression. Mrs. S, age 33, and her husband have been trying to conceive their first child for 2 years.

The couple has undergone infertility workups, including a semen analysis and hysterosalpingography, and results have been within normal limits. The gynecologist recommended intercourse every other day, but Mr. S developed stress-related erectile dysfunction (which was treated with sildenafil).



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Box

Infertility: Medical causes are found in most cases

Infertility affects approximately 6 million U.S. women and their partners.³ As recently as the 1960s infertility was thought to be caused primarily by female psychological problems,⁴ such as neurotic, conflicted feelings about the transition to adulthood or about sex, pregnancy, labor, or motherhood.^{5,6}

This belief changed as researchers identified organic causes of infertility, such as blocked fallopian tubes, sperm abnormalities, and anovulation. A definitive diagnosis can now be made in 85% to 90% of infertility cases, and two-thirds of couples can conceive after medical intervention.⁷

Age and fertility. Most experts recommend that women age >35 who wish to conceive seek gynecologic evaluation after 6 months of unsuccessful intercourse. Chances of becoming pregnant begin to decline at age 35 and drop sharply after age 40.⁸ Beyond age 43, the only infertility treatment likely to be successful is implanting an embryo created with an egg donated by a younger woman.

Mrs. S has no personal or family history of depression. Her depression has worsened as she contemplates more invasive and expensive procedures, such as intrauterine insemination (IUI) and in vitro fertilization (IVF).

Her Beck Depression Inventory score of 22 indicates mild depression. She is not actively suicidal, but she sometimes doubts that life is worth living. She feels like a failure and wants to know if you think stress is contributing to her infertility.

Women with a 2- to 3-year history of infertility despite repeated treatments are at risk of stress, anxiety, and depression.¹ Even if treatment even-

tually succeeds, anxiety often persists during pregnancy.² Your knowledge of medical infertility treatments' emotional toll will help you understand, educate, and support infertile women and their partners.

STRESS AND FERTILITY

Infertility—failure to conceive after 1 year of regular unprotected intercourse—affects approximately 10% of the reproductive-age U.S. population (*Box*).^{3,8} Does stress affect a woman's chance of becoming pregnant? Research into this question—voiced by Mrs. S—has produced conflicting results.^{5,9,10}

Stress does not universally prevent pregnancy; women have conceived as a result of rape. However, chronic extreme stress—such as that imposed by war, imprisonment, or starvation—can change the menstrual cycle. Effects range from subtle luteal-phase deficiency to menses cessation.⁹ It may be that evolution favored females of species who could “turn off” fertility during stressful times to conserve physical resources and “turn it back on” and bear offspring after the threat passed.

Neuroendocrine markers. Researchers examining the role of stress in infertility and its treatments have focused on the neuroendocrine system—particularly neurotransmitters such as prolactin, endorphin, norepinephrine, dopamine, and cortisol. Although chronic anxiety and depression have been linked in animal models to neuroendocrine mechanisms of infertility,⁴ findings in humans have been mixed (*Table 1*).¹¹⁻¹⁵

Psychological interventions. Some investigators have sought to determine whether psychological interventions can increase pregnancy rates in infertile women.

In one prospective, controlled, single-blind study, 184 women who had been trying to conceive for 1 to 2 years were randomly assigned to 10 sessions of group cognitive-behavioral therapy (CBT),

Table 1

Does stress reduce fertility? Research results are mixed

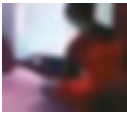
Study design (year of publication)	Results
Controlled prospective trial, 40 women undergoing IVF (1992)¹¹	<p>IVF success rates were comparatively lower among women with high cortisol concentrations</p> <p>Women with high prolactin concentrations had greater numbers of oocytes but lower fertilization rates</p> <p>Failure to conceive was associated with high depression symptom scores, maladaptive coping strategies, and avoidance behavior</p>
Controlled prospective trial, 330 infertile women (1993)¹²	<p>Depressed women had a lower pregnancy rate after a first IVF-ET, compared with nondepressed women</p>
Uncontrolled prospective trial, 13 women without a history of infertility (1997)¹³	<p>Mean adrenaline, norepinephrine, and cortisol levels excreted in urine were not significantly different in menstrual cycles when women conceived, compared with nonconception cycles</p> <p>Little relationship seen between psychological measures of mood state and excretion of adrenaline and cortisol</p>
Controlled, prospective trial, 49 infertile women (1997)¹⁴	<p>Patients who conceived with IVF-ET had lower systolic blood pressures and slower heart rates under stress-test conditions than did those who did not conceive</p>
Controlled prospective trial, 40 women after successful IVF-ET (1998)¹⁵	<p>No difference in hormonal stress markers during first 27 days of pregnancy between women who later gave birth and those who experienced miscarriages</p> <p>Physiologic stress hormone concentrations showed little association with psychological scores, and high anxiety and stress levels did not appear to prevent pregnancy</p>

IVF: In vitro fertilization
IVF-ET: In vitro fertilization with embryo transplant

a standard support group, or usual care. Sixty-four women withdrew before the study ended. After 1 year, women who received psychological interventions—47 in the CBT group and 48 in the standard support group—had statistically significant higher

pregnancy rates, compared with 25 women who received usual care.¹⁶ Conversely, a literature review and evaluation of 25 studies found psychosocial interventions unlikely to improve pregnancy rates in infertile women.¹⁷

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Methodologic problems. Most studies of stress' influence on fertility are small, and many have methodologic problems.⁴ In some, researchers lumped together women whose infertility was caused by disparate diagnoses such as male-factor infertility, blocked fallopian tubes, and advanced age. Retrospective studies also must be interpreted with caution because:

- patients who did not become pregnant may have exaggerated the degree of their depression and its effects
- those with pre-existing medical problems would know they were unlikely to conceive and might have been more depressed before and during infertility treatments.¹⁸

The literature on infertility and stress is dominated by correlational studies. Because of insufficient controlled data, it is unclear whether stress affects the reproductive system.⁴

Recommendation. When counseling patients about the role of stress in infertility and its treatment, we recommend emphasizing that:

- infertility can cause stress in many areas of life
- the effect of stress on fertility, if any, is likely to be minimal for most women.

An infertile woman might respond to psychological counseling or psychotherapy even when a pregnancy is not achieved.^{4,17,19}

CASE CONTINUED: STRAIN AND ANGER

You begin to see Mrs. S weekly for supportive therapy, using cognitive restructuring and relaxation techniques to alleviate her anxiety and depression. She decides not to start an antidepressant because she does not want to be on medication if she becomes pregnant.

During the next 2 months she finishes an unsuccessful IUI cycle and reports that her relationship with her husband has become strained. She avoids friends who have children and feels angry when she sees a pregnant woman. She dislikes going to family events because relatives sometimes ask, "When are you going to get pregnant?"

Her work as a manager is suffering because of her many visits to fertility specialists. Her Beck Depression Inventory score has increased to 33, indicating worsening depression.

Terms such as 'incompetent cervix' and 'old eggs' lead infertile women to blame themselves

INFERTILITY'S PSYCHOLOGICAL TOLL

Patients rarely accept infertility with equanimity, and their responses include shock, denial, anger, isolation, guilt, and grief.⁶ Some women say the experience of being infertile feels comparable to having cancer.²⁰

The incidence of clinical major depression, poor self-esteem, and sexual dysfunction in women who undergo infertility evaluation does not differ significantly from that of their fertile peers.⁹ Even so, infertile women report a roller-coaster ride of emotions: hope as treatments are tried, despair when treatments fail.

Health care providers can add to the angst by telling women they have an "incompetent" cervix, "poor-quality" or "old" eggs, or "inadequate" mucus; these insensitive descriptions can

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Do antidepressants' benefits outweigh the risks?

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lead women to blame themselves and feel ashamed, guilty, and depressed.^{4,5,18}

Psychotherapy. Providing education and teaching skills such as relaxation training has been shown to reduce depressive symptoms more effectively than having patients discuss their thoughts and feelings about infertility.¹⁷ Helpful psychotherapies emphasize CBT and improved coping skills.

Negative coping strategies include escape/avoidance conduct or self-blame (such as, “I’m not getting pregnant because I work too hard”). Encourage patients to replace these with protective coping strategies, such as seeking social support and engaging in active problem-solving (“I reach out to friends who help comfort me, and I set limits with friends who make me feel bad about myself”).²¹⁻²³

Medication. Even though sadness and anxiety are normal responses to infertility, psychotropic medications might be appropriate after a thorough evaluation. Keep in mind, however, that selective serotonin reuptake inhibitors (SSRIs) can cause prolactinemia, which could interfere with ovulation.⁹ Miscarriage and stillbirth rates among women taking SSRIs are similar to those of the general population.²⁴

CASE CONTINUED: IT TAKES TWO

Despite three IUI cycles over 12 months Mrs. S has not become pregnant. She considers IVF but is concerned about the cost and the less than 50% chance of success.

You encourage her to continue individual supportive and cognitive therapy and to consider couple’s therapy. She and her husband decide to attend

Table 2

Fictions and facts about infertility

Fiction	Fact
Infertility is a psychosomatic disorder	An organic cause is found in 85% to 90% of infertile couples ⁷
Infertility is a female problem	One-third of infertility cases are caused by female factors, one-third by male factors, and one-third by male and female factors or unknown causes ²⁶
Infertility is epidemic	The number of patients seeking infertility treatment has increased dramatically in 20 years, but the infertility rate is stable ^{3,5,18}
Infertility is rare	Approximately 10% of U.S. couples of childbearing age are infertile ³
If you adopt, you'll get pregnant	Conception rates are no higher following adoption than among childless couples ⁷

a group for couples with infertility. She accepts your referral to RESOLVE, a national support program for infertile patients (see *Related resources*).

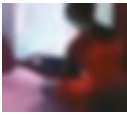
PROBLEMS FACING INFERTILE COUPLES

Gender differences in coping style. Men and women experience infertility differently.

The women in infertile couples often are distressed, whereas the men tend to remain more confident that some kind of treatment will work. This imbalance can leave the woman feeling unsupported and the man feeling confused about why she is so upset about what he sees as just a medical problem to be solved.

When a couple’s infertility has been attributed to sperm abnormalities, however, the man’s stress level can equal the woman’s. Women tend to feel stress regardless of which partner is “at fault.”²⁵

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Grief reactions. The “loss” of a child never conceived generally goes unrecognized but has psychological consequences. Both partners can feel:

- low self-esteem
- sadness about being unable to experience parenting
- doubts about their femininity or masculinity
- regret over unfulfilled dreams.

These feelings can be exacerbated by well-meaning relatives and friends who offer misguided advice such as, “Just relax,” or “Quit your job; then you’ll get pregnant” (*Table 2, page 71*).^{3-5,7,18,26} Couples might begin to resent relatives and avoid family gatherings, especially if they anticipate being questioned about children. They might become jealous of siblings who have children. Infertile women might begin to avoid social interactions.

Sexual activity is no longer pleasurable for many couples going through infertility treatments, and the loss of intimacy can strain the marriage. Sex becomes an obligation devoid of spontaneity, excitement, and enjoyment.⁴ Regimentation—such as physician advice about when the couple should and should not have sex—can lead to sexual dysfunction.

In vitro fertilization averages \$12,400 per cycle, and less than 50% of women conceive

Employment. Infertility treatments are time- and resource-intensive, and patients often miss work. Even while on the job, a woman distracted by infertility or treatment side effects might not perform as well as she could. Worries about job security add to her anxiety.

Finances. Infertility treatment is expensive and is not always covered by insurance. The American Society for Reproductive Medicine reports that the cost of an IVF cycle averages \$12,400, and success rates are <50%. In

2003, the chances of delivering a living child following IVF ranged from 21% to 43% per cycle for women age <40 years²⁶ (see *Related resources*).

To continue treatment, couples may take second jobs, acquire loans, deplete savings, or accumulate debt. Many couples—even with extraordinary effort—cannot afford to start or continue advanced infertility treatments.

Spirituality. Patients who believe that infertility is God’s punishment for past sins may experience a religious crisis. Those affiliated with religions that restrict assisted-reproductive technology may feel forced to choose between doctrinal dictates and their dreams of becoming parents.

CASE CONTINUED: A NEW ‘RESOLVE’

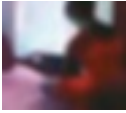
Mrs. S enjoys her association with the online support of RESOLVE. Through message boards, she shares her concerns with other women undergoing infertility treatment. She also finds support from friends, although she continues to set limits such as declining invitations to baby showers. She practices relaxation techniques at home.

Since she and her husband have joined the group for infertile couples, their relationship has improved. Mrs. S feels that he better understands her fears after hearing other women in the group being “just as emotional.” He no longer tells her, “It’s just a medical problem.”

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Stress appears to have minimal effect on fertility, but infertile women often report stress, anxiety, and depression. Helpful psychotherapies emphasize relaxation training, cognitive-behavioral therapy, coping skills, and support networks. Consider couples’ therapy to address the sexual, social, and financial strain associated with infertility treatments.

BottomLine



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 Related resources

- ▶ National Infertility Association (RESOLVE). www.resolve.org.
- ▶ American Society for Reproductive Medicine. www.asrm.org.

DRUG BRAND NAME

Sildenafil • Viagra

DISCLOSURES

The authors report no financial relationship with any company whose products are mentioned in this article or with manufacturers of competing products.

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