

Infertility's dark moods

Couples who try but repeatedly fail to conceive a child can end up exploring the far reaches of anguish. A new study suggests, in a reversal of this sequence, that women who experience bouts of depression in the months or years before trying to get pregnant have a substantially greater chance of encountering infertility.

"Our data suggest that depressive symptoms as well as the drugs used to treat these conditions may play an important role in the [causation] of infertility in women," contend Kate L. Lapane, a psychologist at Memorial Hospital of Rhode Island in Pawtucket, and her colleagues. They report their findings in the November-December *PSYCHOSOMATIC MEDICINE*.

The researchers administered questionnaires to 339 women age 22 to 47 who had participated in health surveys conducted in the Pawtucket area during the 1980s.

Of 58 women who cited a history of depressive symptoms—periods of feeling so sad, discouraged, hopeless, or burdened by problems that they "wondered if anything was worthwhile"—14 reported infertility. Lapane's team defined that condition as the inability to get pregnant for at least 1 year with a partner known to be able to conceive a child.

In contrast, only 38 of 281 women noting no prior periods of depression reported infertility. In other words, previously depressed women exhibited about twice the infertility rate of nondepressed women. This difference remained when the investigators controlled statistically for cigarette and alcohol use, antidepressant drug use, weight, amount of physical exercise, and sexually transmitted diseases in the past.

Infertility also showed a strong independent association with imbibing any amount of alcohol at least twice a week and with the prior use of antidepressants.

Although the study is far from conclusive, "depression may be an important factor to consider in future studies of infertility," write David R. Rubinow and Catherine A. Roca, both psychiatrists at the National Institute of Mental Health in Bethesda, Md., in an accompanying editorial.

Other evidence indicates that depressed women who undergo in vitro fertilization or embryo transfers get pregnant far less often than nondepressed women, Rubinow and Roca point out. Depression sparks a variety of hormonal and immune system changes that may contribute to infertility, they suggest.

Depressed kids in China

About 1 Chinese child in 10 displays symptoms of severe depression, a proportion that closely matches depression estimates for U.S. youngsters, scientists report in the December *JOURNAL OF CONSULTING AND CLINICAL PSYCHOLOGY*.

As in the West, depressed children in China—especially boys—display behavior problems, lag behind academically, and make few friends, the researchers assert. However, they note that extreme shyness and sensitivity to others appears more typical of childhood depression in the West than in China. They relate the difference to the greater value placed on shy, reticent, and emotionally inhibited behavior in Chinese culture.

Xinyin Chen, a psychologist at the University of Western Ontario in London, directed a survey of 261 children selected at random from three Shanghai primary schools. The youngsters were examined at age 8 and again at age 10. Their parents, teachers, and classmates also completed questionnaires.

Social feedback may channel the course of childhood depression in China, Chen's group argues. For instance, the presence of a warm, accepting mother buffered children with academic problems at age 8 from developing depression at age 10. They speculate that peer relations also loom large: Chinese students must evaluate classmates and themselves regularly, and their social and academic standings are publicized.

Ovulation heralds end of fertile period

The timing of ovulation has taken on a new significance for couples who are trying to get pregnant. While the release of an egg from a woman's ovary still marks the peak time for fertilization, it's also the start of a rapid decline in a woman's ability to become pregnant, according to a new report.

A study of 221 healthy women age 25 to 35 shows that for the highest chance of pregnancy, intercourse must occur during the 5 days before ovulation; the probability peaks on the day of ovulation. The chance of pregnancy then drops to almost zero the following day.

"It is surprising how rapidly it goes from maximal fertility to almost zero fertility," says study investigator Clarice R. Weinberg of the National Institute of Environmental Health Sciences (NIEHS) in Research Triangle Park, N.C. "It is unusual in any biological system to see something that abrupt."

Conventional wisdom has held that optimal fertility occurs during the few days before and after a woman ovulates. However, laboratory studies of fertilization indicate that eggs remain viable for only 12 to 24 hours. Sperm, on the other hand, retain their ability to fertilize eggs for up to 5 days in the female reproductive tract.

None of the women in the NIEHS study had experienced fertility problems. The researchers analyzed hormones in daily urine samples to pinpoint the day of ovulation and compared that record with a history of intercourse to determine the day fertilization most likely occurred.

Weinberg and study leader Allen J. Wilcox report in the Dec. 7 *NEW ENGLAND JOURNAL OF MEDICINE* that 76 percent of the 192 pregnancies occurred when the couple had intercourse on the day of ovulation or the 2 days before. Only a few occurred when intercourse took place on the day after ovulation.

"Our findings could be explained by a short period of viability for the egg," says Weinberg. "Or hormonal changes following ovulation could change the cervical mucus such that sperm cannot penetrate it."

Weinberg notes that they studied a relatively small number of women, so the group's findings need to be confirmed. In the meantime, she plans to study the hormonal factors that may determine whether an ovulation cycle will lead to pregnancy.

IL-12 studies back on track

Last June, the U.S. Food and Drug Administration halted a test of the promising anticancer and anti-AIDS drug interleukin-12 (IL-12) after two patients died and several others suffered severe side effects from dosages previously demonstrated to be safe. At the time, scientists at the company conducting the study, Genetics Institute in Cambridge, Mass., speculated that the long-acting form of the drug may have caused the toxic effects (*SN*: 6/17/95, p.375).

Now, after animal studies, the researchers conclude that the problem lies not in the formulation but in the timing of doses. In the original clinical trials, one dose of IL-12 was given to patients so researchers could determine how fast the body eliminated it. After a few weeks, the volunteers took various doses regularly—once a day, for example. In the halted trial, researchers gave participants, who suffered from kidney cancer, a high, but presumed tolerable, regular dose from the outset.

In tests, the company scientists found that for unknown reasons they had to prime the animals with a single dose of IL-12 a few weeks before starting them on a multiple-dose schedule of the drug. Presented with these results on Oct. 18, FDA lifted the clinical hold on the trial. The company resumed human trials of IL-12 for cancer and AIDS last month.

"We are still investigating why this schedule effect is taking place," says company spokeswoman Gina Brazier. "It has never been seen before in any drug."