Newly Invented Endometrial Function Test (EFT®) Solves the Puzzle of Unexplained Infertility

A Yale researcher who invented a test to determine whether a woman’s endometrium (uterine lining) is healthy and ready for embryo implantation has identified two new biochemical markers that improve assessment of the endometrium.

The endometrial function test (EFT®) was created by Harvey J. Kliman, M.D., a research scientist in the Department of Obstetrics, Gynecology and Reproductive Sciences at the Yale School of Medicine. An abnormal EFT is associated with pregnancy failure, while a normal EFT is associated with pregnancy success. Kliman’s study, published in the July issue of the journal Fertility and Sterility, identifies two new biochemical markers, cyclin E and p27, that more accurately assess endometrial health compared to the routine examination that is done by pathology laboratories.

"These findings will help women who have difficulty conceiving become pregnant at a reduced cost," said Kliman who likens the endometrium to soil and the embryo to a treasured plant. "Soil has to be tested and prepared in order for the plant to grow in it. The endometrium also has to be healthy and capable of supplying the appropriate nutrients for the embryo. If the right conditions do not exist, implantation will not occur. This test, which uses these new biochemical markers, will improve assessment of the endometrium."

Kliman said the most difficult step in the process of conception is the attachment (implantation) of the embryo to the endometrium. Abnormalities in the process of implantation are believed to be the basis of many cases of unexplained infertility in women. A normal healthy endometrium will make many different substances (markers). By measuring several of these markers in endometrial biopsies, researchers can determine if the endometrium is receptive to implantation. Kliman said the two new markers he used in his study are more effective at assessing endometrial health than the other markers studied to date or methods in current use.

"It is important that patients and doctors know that this test is available," said Kliman. "The EFT helps a patient and doctor figure out what the next steps are when assisted reproductive technology procedures don’t appear to work. The test is done only at Yale, and we currently receive biopsies from all over North America for evaluation."

In this initial study, Kliman and his colleagues looked at 33 fertile volunteers, 83 women seeking fertility treatment, and 23 women undergoing mock cycles in preparation for frozen or donor embryo transfer. The researchers compared the expression of cyclin E and p27 in these groups at many different times throughout the menstrual cycle to establish the normal and abnormal patterns of expression of the markers in the endometrium.

The endometrium is made up of stroma and glands. The endometrial stroma is the tissue that supports the glands and holds the endometrium together, much like the cake supports the fruit in a fruitcake. "Fertile women expressed cyclin E in their glands up to about cycle day 19, and then did not have any after that," said Kliman. "Infertile women, on the other hand, much more frequently expressed cyclin E well after cycle day 19, often to the end of their cycles. The stroma in both groups was the same. These results suggest that infertile women have a defect in the way the stroma communicates with glands."

Kliman said a normal endometrium is like a surfer and a wave she has caught — with the wave being the stroma and the surfer the glands. "Just as the surfer will miss the wave if it goes by too quickly, the endometrial glands can be left behind if the stroma moves too quickly," said Kliman. "This is what happens in many women with unexplained infertility. The EFT® can diagnose this problem and help guide the infertility specialist to fix the problem, which in turn will improve the chances of implantation and a successful pregnancy."

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