Surgeons Recreate Eggs To Treat Infertility

Regenerative medicine researchers have moved a promising step closer to helping infertile, premenopausal women produce enough eggs to become pregnant. Surgeons at Wake Forest Baptist Medical Center's Institute for Regenerative Medicine in Winston-Salem, NC, reported that they were able to stimulate ovarian cell production using an in vitro rat model, and observed as the cells matured into very early-stage eggs that could possibly be fertilized. Results from this study were presented at the 2012 American College of Surgeons Annual Clinical Congress.

"While conventional hormone replacement therapy is able to maintain female sexual characteristics, it's unable to restore ovarian tissue function, which includes the production of eggs," the study's authors reported. Ovarian tissue function is critical for premenopausal women who desire to conceive.

Several fertility disorders can leave premenopausal women without an adequate amount of eggs. These disorders can also prevent a woman's ovaries from secreting enough of the hormones that stimulate egg production. Events such as ovarian operations, an injury, or radiation therapy for cancer can interfere with ovarian function, according to Anthony Atala, MD, FACS, director of the Wake Forest Institute for Regenerative Medicine and chair of the department of urology at the Wake Forest Baptist Medical Center.

According to Dr. Atala, the goal of this study was to spur the ovaries to produce the female sex hormones estrogen and progesterone as well as stimulate egg production. The surgeons extracted ovarian cells from three-week old female rats, which would be equivalent to about 25 years-old in humans. The cells were isolated in a culture of nutrient-dense growth factors for one week. Next, the cells were placed under a collagen gel that allows them to grow three dimensionally instead of in a single layer. The researchers then assessed cell growth, hormone production, and gene expression in the specimens.

In their early observations, the surgeons found immature oocytes protruding from clusters of ovarian cells. To help the oocytes mature, the surgeons developed a microwell system to keep oocytes inside clusters of ovarian cells. In humans, primordial germ cells or oogonium are the first stage of development into ovums, or mature eggs. The researchers also found that the cells expressed germ cell markers consistent with those of early stage eggs. They observed that the oocytes began to develop zona pellucida, a membrane that forms around an ovum as it develops, and showed a capacity to produce steroids similar to those produced by early stage eggs or follicles.

"Now, the goal is creating more mature structures that could actually be used for fertilization," Dr. Atala explained.

Dr. Atala and his colleagues believe that the newly generated oocytes would be able to mature to a certain stage in humans. The oocytes would then be put back into the female patient to go through natural ovulation and conception, or the oocytes would be fertilized in vitro and then implanted in the uterus. Dr. Atala said because ovarian cell function is restored, a woman using this procedure may be able to produce the necessary hormones and would not need additional hormone replacement therapy.

Although the surgeons were able to generate early stage eggs in vitro, Dr. Atala cautions that the procedure has a while to go before it can be applied to humans: "This study represents the elementary, first stages of the research process," he said. "But we're showing the principle signs that this approach is a potential strategy for infertile women who want to have children," he concluded.

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