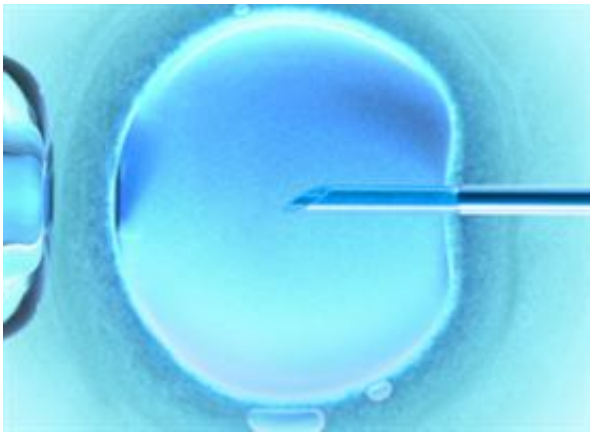
Study shows male hormones play an important role in female fertility

March 4 2014, by Emily Boynton



(Medical Xpress)—Several fertility clinics across the country are beginning to administer testosterone, either through a patch or a gel on the skin, to increase the number of eggs produced by certain women undergoing in vitro fertilization (IVF). Women are also purchasing the over-the-counter supplement DHEA, which is converted by the body into testosterone, to boost their chances of pregnancy with IVF.

A few clinical trials support the use of testosterone given through the skin, while others have shown no benefit of DHEA – also used in attempts to slow aging and enhance muscle mass – in increasing pregnancy and birth rates in women who don't respond well to IVF therapy. Lacking a large and convincing body of data on the topic, the

jury is still out as to whether male hormones such as testosterone improve female fertility.

A new study suggests that male hormones, also called androgens, help drive the development of follicles – structures that contain and ultimately release an egg that can be fertilized by a man's sperm. Published in the *Proceedings of the National Academy of Sciences*, the research also details how male hormones boost the production of follicles in mice. Authors believe the study provides potential biological targets to enhance fertility in women with diminished ovarian reserve, who produce few or no follicles in response to IVF drugs designed to boost follicle development.

"There is a raging debate in the reproductive endocrinology field about what male hormones are doing in female fertility," said Stephen R. Hammes, M.D., Ph.D.,senior study author and professor of Endocrinology at the University of Rochester School of Medicine and Dentistry. "Our study doesn't solve the controversy, but, along with some earlier seminal studies from other groups, it does tell us that we can't dismiss male hormones. They might actually be doing something useful."

Using multiple animal models and cell experiments, Hammes and lead study author Aritro Sen, Ph.D., research assistant professor of Endocrinology at the medical school found that male hormones promote follicle development in two ways. First, they prevent follicles from dying at an early stage. They do this by ramping up a molecule that stops cells from self destructing, a process called apoptosis. Hammes and Sen speculate that if a woman doesn't have enough androgens (male hormones), more of her follicles may be dying and fewer progressing to a mature stage when they produce and release an egg.

Second, androgens make ovarian cells more sensitive to follicle-stimulating hormone or FSH, which promotes follicle growth. They do

this by creating more FSH receptors – molecules on the surface of ovarian cells that jumpstart the follicle making process in response to the hormone.

"Androgens are increasing follicle growth and ensuring follicles don't die – exactly what you want when providing fertility treatment," noted Hammes, who is also the chief of the Division of Endocrinology and Metabolism at UR Medicine's Strong Memorial Hospital.

When the team administered small doses of androgens to mice that were taking the equivalent of medications given to women undergoing IVF therapy, they developed more mature, egg-containing follicles than mice that didn't receive androgens. The androgen-treated female mice also released larger numbers of eggs with ovulation. IVF drugs are designed to do just that, enhance ovulation – the production and discharge of an egg or eggs from the ovary. Unfortunately, these drugs aren't always effective in women with diminished ovarian reserve.

Kathleen M. Hoeger, M.D., M.P.H., director of UR Medicine's Strong Fertility Center, estimates that around 20 percent of the patients her team treats have diminished ovarian reserve, meaning they produce fewer follicles than estimated based on their age. Women who are 40 years or older are most likely to have diminished ovarian reserve, but it can appear in younger women as well.

"This information is important because it provides theoretical support for administering androgens to some women undergoing IVF, a practice that our fertility clinic and many others across the country have started in recent years," said Hoeger, who is also a professor of Obstetrics and Gynecology at the School of Medicine and Dentistry. "If these data are confirmed in clinical trials, we could propose that raising low levels of androgens in a woman with diminished ovarian reserve might increase her ability to produce more and better eggs for fertilization."

Hammes says the study calls for further clinical trials to determine whether androgens can have a positive effect on fertility when given at the right doses. And, by better understanding the biological pathways that are important for follicle development, scientists may be able to target these pathways with drugs or other interventions to improve IVF success rates.

More information: Androgens regulate ovarian follicular development by increasing follicle stimulating hormone receptor and microRNA-125b expression, www.pnas.org/content/111/8/3008.abstract

Provided by University of Rochester Medical Center