

Most Young Women with Menopause-like Condition Retain Store of Eggs

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(PhysOrg.com) -- Contrary to what researchers had previously believed, most young women and girls who experience a menopause-like condition called primary ovarian insufficiency still have immature eggs in their ovaries, according to a study by scientists at the National Institutes of Health.

Primary ovarian insufficiency, or POI, results in a menopause-like condition years before normal menopause begins—sometimes as early as the teens and twenties. [Women](#) with primary ovarian insufficiency stop producing normal amounts of reproductive hormones, develop hot flashes, and typically become infertile.

"The discovery that most women with primary ovarian insufficiency have immature eggs remaining in their ovaries raises the possibility of developing treatments for the infertility that accompanies the condition," said Alan E. Guttmacher, M.D., acting director of the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD), the NIH institute at which the study was conducted.

The findings were published online in [Fertility and Sterility](#). The study's senior author was Lawrence M. Nelson, M.D., head of NICHD's Integrative Reproductive Medicine Group.

POI occurs in 1 out of 100 women by age 40. In addition to experiencing hot flashes, women with POI cease having regular menstrual periods. The symptoms may be lessened or relieved by therapy to replace the

missing hormones. Although most women with POI are infertile, Dr. Nelson said, about 5 to 10 percent become pregnant unexpectedly at some time after their condition is diagnosed.

The findings expand on earlier research showing that ovulation is possible in this group of patients. Refinement in ultrasound technology allowed the researchers to detect ovarian follicles in three quarters of the POI patients who took part in the study.

For the current study, Dr. Nelson and his colleagues used ultrasound to assess follicle maturation in a group of women with POI. A follicle is a fluid-filled sac in the ovary that gives rise to the egg cell. The researchers compared 97 women who had POI with 42 women with normal menstrual cycles. When the scientists performed ultrasound examinations on the women with POI, they were surprised to discover that 73 percent of the women had ovarian follicles. Moreover, these follicles were capable of producing ovarian hormones.

Dr. Nelson explained that during a normal menstrual cycle, the pituitary gland releases follicle-stimulating hormone (FSH), which causes follicles to grow. While they are growing, follicles release the hormone estradiol, a form of estrogen. The pituitary also produces another hormone, called luteinizing hormone (LH), which remains at low levels during most of the cycle and then surges when it is time to ovulate. This LH surge gives the follicle a signal to break open and release the egg.

The scientists found that in women with primary ovarian insufficiency, both FSH and LH levels are higher than in women without the condition.

"The high LH levels indicate that the pituitary is continually sending the [ovaries](#) the message to ovulate," Dr. Nelson said. "The follicles get the message to mature before they are ready, and so they don't grow normally, and in most cases, fail to release the egg."

In women of reproductive age who do not have POI, the ovary produces what Dr. Nelson refers to as a support group of extra follicles. These extra follicles develop along with the dominant follicle—the one that eventually releases the egg. Dr. Nelson theorizes that the extra follicles produce estradiol and other hormones to provide negative feedback to the pituitary. The hormones from the support group follicles regulate the pituitary, keeping FSH and LH blood levels in the normal range. In an [earlier study](#), Dr. Nelson and his colleagues found that most women with POI do not have the follicle support group.

Without the support group, Dr. Nelson said, the solitary dominant follicle fails to mature properly due to the high LH levels. The patients develop what Dr. Nelson refers to as lonely luteinized follicles.

In the current study, women with primary ovarian insufficiency had lower levels of estradiol than women with normal menstrual cycles. But the women's follicles were producing some estradiol, the scientists found, and they had higher levels of estradiol than did women who had no detectable follicles. They also had higher levels of progesterone, a hormone that follicles produce in response to LH.

"These follicles aren't inert structures," Dr. Nelson said. "They are producing reproductive hormones—just not enough."

Women with primary ovarian insufficiency are usually treated with a patch that releases estradiol to alleviate their menopause-like symptoms. In a few instances, participants in Dr. Nelson's studies at NIH have become pregnant during their treatment with the estradiol patch. Dr. Nelson hypothesizes that the estradiol supplied by the patch allowed their follicles to mature by suppressing LH levels into the normal range. He is planning a study to determine if, in addition to relieving their menopause like symptoms, the replacement estradiol supplied by the patch will also improve their chances of ovulation.

"The body needs estradiol both to prepare the lining of the uterus to support pregnancy and also to regulate FSH and LH levels in a feedback loop," Dr. Nelson said. "We hope to test whether giving estradiol via a skin patch to women with primary ovarian insufficiency will tamp down their LH level, allow the follicles to mature at an appropriate time, and help women with this condition to ovulate."

Dr. Nelson thinks that the one-quarter of the women in his study who did not have follicles that could be detected by ultrasound may simply have been observed at a time when the follicles were not growing. If the women were examined on another occasion, follicles may have been visible, he said. With POI, ovarian functioning appears to be intermittent and unpredictable. So the fact that the researchers were unable to detect follicles in some of the women during the study doesn't preclude that on another occasion the women would develop follicles large enough to be detected by ultrasound.

In [previous research](#), Dr. Nelson and his coworkers reported that women who experience a delay in diagnosing POI have an increased risk of low bone density.

"It's really important for women with POI to get a diagnosis as soon as possible so they can begin treatment," he said. "Lack of reproductive hormones may result in bone thinning and, possibly, bone fractures, later in life."

Provided by National Institutes of Health

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