

Plan offers guidance for evaluating menopause-like condition in girls and young women

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A comprehensive plan to help health care professionals diagnose and treat primary ovarian insufficiency—a menopause-like condition affecting girls and young women that may occur years before normal menopause is expected—has been developed by a scientist at the National Institutes of Health.

Lawrence Nelson, M.D., head of NIH's Integrative and Reproductive Medicine Unit, provided recommendations based on the research he has conducted at the NIH. His recommendations are published in the Clinical Practice feature of the February 5 *New England Journal of Medicine*.

In primary ovarian insufficiency, the ovaries stop releasing eggs and producing estrogen and other reproductive hormones. The sudden cessation of ovarian function results in a condition similar to that of normal menopause: loss of menstrual periods, infertility, hot flashes and night sweats, sleep loss, and increased risk for bone fracture and heart disease. The sudden and unexpected loss of fertility frequently results in feelings of grief, anxiety and depression.

Treatment consists of hormones to replace those no longer produced by the ovaries and counseling to help women cope with the grief, anxiety, and depression that may result from the diagnosis and the loss of fertility.

"The early indicators of primary ovarian insufficiency are subtle and the condition can be difficult to diagnose," said Duane Alexander, M.D., director of NIH's Eunice Kennedy Shriver National Institute of Child Health and Human Development, where Dr. Nelson conducts his research. "Dr. Nelson's report provides helpful information for health care professionals and patients on how to recognize the early symptoms of the condition so that women can benefit from prompt diagnosis and early treatment."

Because ovulation may sometimes occur in this group of women, primary ovarian insufficiency is more accurate than other terms that have been used to describe the condition, such as premature menopause or premature ovarian failure, Dr. Nelson wrote. Primary ovarian insufficiency occurs in women younger than age 40—the age at which menopause may begin.

A woman can be considered to have primary ovarian insufficiency if she has not experienced a menstrual cycle in 4 months or more, and if at least two tests taken more than 1 month apart show that she has abnormal levels of follicle stimulating hormone (FSH). FSH is produced by the pituitary and stimulates the ovaries to produce estrogen and prepare an egg for release.

Specifically, girls and young women with primary ovarian insufficiency have high FSH levels like those of women in menopause.

Dr. Nelson wrote that in rare instances, primary ovarian insufficiency may resolve spontaneously, and normal menstrual cycles and fertility will be restored. In 5 to 10 percent of cases, women become pregnant after having been diagnosed with primary ovarian insufficiency.

Dr. Nelson outlined a number of steps health care professionals can take to identify potential causes for the cessation of a woman's menstrual

cycle. These include learning whether the woman has an underlying disease or condition, is exercising excessively and perhaps eating too little, or has had prior chemotherapy or radiation therapy. The diagnosis of primary ovarian insufficiency is made largely by the presence of FSH levels in the menopausal range. Once the diagnosis is made, additional tests for various chromosomal conditions and hormonal abnormalities should also be performed.

Dr. Nelson added that it is not appropriate to attribute missing or irregular menstrual periods to stress without further evaluation.

"A disordered menstrual cycle should be viewed as a vital sign that something could be wrong and a signal indicating the need for further evaluation," Dr. Nelson said.

Dr. Nelson wrote that 4 months or more of missing, irregular, too few, or too frequent, menstrual periods merit further evaluation.

In 90 percent of cases, the cause of primary ovarian insufficiency is unknown. In the remainder of cases it can be attributed to a genetic condition or to autoimmunity—a condition in which the immune system attacks the body's own tissues. Women in families affected by Fragile X syndrome—an intellectual disability resulting from an abnormality on the X chromosome—are at increased risk for primary ovarian insufficiency.

The unexpected loss of fertility that accompanies primary ovarian insufficiency can be emotionally devastating for many women, Dr. Nelson wrote. Patients should be monitored for signs of severe emotional distress and, when appropriate, referred for counseling or other sources of emotional support.

Earlier research has found that treatment with the hormones estrogen

and progestin to relieve the symptoms of menopause increases the risk of heart disease. Dr. Nelson noted that the results of that research do not apply to girls and women with primary ovarian insufficiency, who are too young to have undergone normal menopause. He added that most health care professionals agree that treatment with estrogen and progestin is appropriate for women with primary ovarian insufficiency, to replace the hormones their bodies would otherwise produce.

Pregnancy is unlikely in primary ovarian insufficiency but does sometimes occur, so sexually active women with the condition should be aware of this possibility. Dr. Nelson added that some evidence indicates that oral contraceptives may not be effective for this group of women, and so they need to rely on other forms of contraception.

Because women with primary ovarian insufficiency are at risk for low bone mineral density, they should also be advised to consume adequate calcium and vitamin D, and to get sufficient exercise, methods which have been proven to safeguard bone health.

Source: NIH/National Institute of Child Health and Human Development

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