

Female Infertility Caused by Disorders of the Ovulation Process

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Annotation: A marriage is considered infertile in which, despite regular sexual activity for a year without the use of any contraceptives, pregnancy does not occur, provided that the spouses are of childbearing age. The time required for pregnancy increases with age; for women over 35 years of age, consultations with an obstetrician-gynecologist for examination and treatment should begin after 6 months of unsuccessful attempts at natural conception. However, diagnosis may be initiated earlier in women with irregular menstrual cycles or known risk factors for infertility, such as endometriosis, a history of pelvic inflammatory disease or malformations of the reproductive tract.

Keywords: female infertility, ovulation, conception, menstrual cycle.

Introduction. Women can have infertility if the ovaries do not release an egg every month, as they usually do during the menstrual cycle. Ovulation may not occur at all or occur irregularly if certain hormones are not released from the brain or ovaries in violation of the normal monthly cycle.

Women can determine if and when ovulation occurs by measuring body temperature or using an ovulation prediction kit at home. Doctors use ultrasound or blood or urine tests to assess ovulation problems. Medications, usually clomiphene or letrozole, can be used to stimulate ovulation.

Ovulation is the release of an egg from the ovary. It usually occurs in the middle of the menstrual cycle. A normal cycle takes from 24 to 38 days. In women, a common cause of infertility is a problem with ovulation.

The female reproductive system is controlled by hormones produced by areas of the brain, including the hypothalamus (the area of the brain that coordinates and controls hormonal activity) and the pituitary gland, as well as the ovaries. The hormonal interactions that control ovulation and the menstrual cycle have the following sequence:

Gonadotropin-releasing hormone (GnRH) is released from the hypothalamus.

GnRH stimulates the pituitary gland (also located in the brain).

The pituitary gland releases luteinizing hormone (LH) and follicle stimulating hormone (FSH).

LH and FSH (hormones that control ovulation) stimulate the ovaries.

The ovaries produce the female sex hormones estrogen and progesterone, which control the menstrual cycle.

Problems with ovulation (egg release) occur when one of the parts of this system does not function properly. Ovulation can be disrupted if any of these stages or hormones do not match the norm. Ovulation can also be affected by abnormalities in the work of other hormonal glands, such as the adrenal glands or thyroid gland.

Problems with ovulation can be caused by many diseases.

The most common cause of chronic ovulation problems is:

polycystic ovary syndrome, which is the cause of irregular menstruation, and often also leads to excessive weight gain, acne and/or excessive body hair (due to excessive production of male hormones by the ovaries).

Other causes of ovulation problems include:

diabetes mellitus;

Fatness

Hyperthyroidism

Hypothyroidism

excessive exercise;

some medications (including estrogens and progestins, as well as some antidepressants);

excessive weight loss;

depression.

In rare cases, the cause is premature menopause — when the supply of eggs in the ovaries turns out to be low at an age less than average, (the average age of menopause is 51 years).

Women with ovulation problems may lack menstruation (amenorrhea) or have irregular bleeding called abnormal uterine bleeding.

Tracking the timing of menstrual cycles

a set for predicting ovulation at home;

Sometimes a daily measurement of body temperature;

ultrasound examination.

The doctor asks the woman to describe her menstruation (menstrual history), including the frequency and duration of menstruation. Based on this information, the doctor can determine whether a woman is ovulating.

Ovulation prediction kits at home are the most accurate method that can be used at home, but they do not have 100% accuracy, so some ovulations may be missed. This kit determines an increase in the level of luteinizing hormone in the urine 24-36 hours before ovulation. To get a more accurate result, some kits also measure estrogen byproducts. Urine analysis is performed for several days in a row in the middle of the menstrual cycle.

Another method for determining whether a woman is ovulating is a woman's daily measurement of her temperature at rest (measurement of basal body temperature). Usually the best time is the period immediately after waking up and before going to bed. A decrease in basal body temperature suggests that ovulation should occur soon. If possible, she should use a thermometer to measure basal body temperature, designed specifically for women trying to get pregnant, or an electronic or mercury thermometer. An increase in temperature of 0.5 °C or more usually indicates that ovulation has recently occurred. However, this method is time-consuming and is not reliable or accurate.

The doctor can accurately determine whether ovulation has occurred and when it occurs. The following methods are used

Ultrasound

is a measurement of the level of progesterone in the blood or the level of one of its byproducts in the urine.

a marked increase in the level of progesterone or its conversion products indicates that ovulation has occurred.

The doctor may perform other tests to determine the abnormalities that led to problems with ovulation. For example, testosterone levels in the blood can be measured to determine polycystic ovary syndrome.

Treatment of the cause, if it is identified;

a drug for ovulation stimulation.

When major diseases are detected (for example, polycystic ovary syndrome or too high prolactin levels), their treatment is carried out.

Ovulation can usually be stimulated by medications such as letrozole, clomiphene, or human gonadotropins. The choice of a particular drug depends on the specific problem. If the cause of infertility is premature menopause, neither clomiphene nor human gonadotropin will be able to stimulate ovulation.

Letrozole

Letrozole is often the drug of choice used to stimulate ovulation, as letrozole has fewer side effects than clomiphene, another widely used ovulation stimulation drug. The most common side effects of letrozole are fatigue and dizziness.

Letrozole is an aromatase inhibitor. Aromatase inhibitors block the production of estrogens. They are also used to treat breast cancer in menopausal women.

In women with polycystic ovary syndrome and obesity, letrozole may be more likely to stimulate ovulation than clomiphene. In other women, studies have not shown that letrozole is more effective than clomiphene.

The intake of letrozole begins a few days after the onset of menstruation, the woman takes the drug orally for 5 days. If ovulation does not occur, a higher dose of clomiphene is used in each cycle until ovulation occurs or the maximum allowable dose is reached.

Letrozole is prescribed only after receiving a negative pregnancy test result, since when taken in the early stages of pregnancy, it can cause congenital malformations.

Clomiphene

In addition, doctors may prescribe clomiphene. Clomiphene is most effective when the cause of ovulation problems is polycystic ovary syndrome.

A few days after the start of menstruation, a woman takes clomiphene orally for 5 days. Before starting a medication, a woman usually needs to be prescribed hormones to cause menstrual bleeding. Ovulation usually occurs 5-10 days after the end of clomiphene intake, and menstruation begins 14-16 days after ovulation.

If menstruation does not begin after treatment with clomiphene, a pregnancy test should be performed. If pregnancy has not occurred, then the treatment cycle is repeated. A higher dose of clomiphene is used in each cycle until ovulation occurs or the maximum allowable dose is reached. When the dose stimulating ovulation is determined, the woman takes this dose before 4 additional cycles of treatment. In most women, pregnancy occurs by the fourth cycle, in which ovulation occurs. Although ovulation occurs in 75-80% of women after taking clomiphene, pregnancy occurs only in 40-50% of women. Approximately 5% of women who become pregnant after taking clomiphene become pregnant with more than 1 fetus (multiple pregnancy), usually twins.

Side effects of clomiphene include hot flashes, bloating, breast tenderness, nausea, visual disturbances and headaches.

Ovarian hyperstimulation syndrome develops in less than 1% of women treated with clomiphene. In this syndrome, the ovaries are significantly enlarged, and a large amount of fluid increases blood flow in the abdominal cavity. This syndrome can be life-threatening. To try to prevent it, doctors prescribe the minimum effective dose of clomiphene, and when the ovaries are enlarged, the drug is canceled.

Clomiphene is prescribed only after receiving a negative pregnancy test result, since when taken in the early stages of pregnancy, it can cause congenital malformations.

Metformin

To stimulate ovulation, doctors may prescribe metformin (a drug that is also used to treat diabetics) to some women. Metformin is often prescribed to women with polycystic ovary syndrome, especially those who also have obesity (with a body mass index of 30 or higher) and/or diabetes or prediabetes (blood sugar levels are high, but not enough to be considered diabetes). But even in these women, clomiphene is usually more effective than metformin in terms of ovulation stimulation, and is just as effective as metformin in combination with clomiphene.

Human gonadotropins

If a woman does not ovulate or become pregnant during treatment with clomiphene and letrozole, then hormonal therapy with human gonadotropins, which can be administered intramuscularly or subcutaneously, can be performed. Human gonadotropins contain follicle stimulating hormone and sometimes luteinizing hormone. These hormones stimulate the maturation of follicles in the ovaries and thereby make ovulation possible. Follicles are fluid—filled cavities, each of which contains an egg. With the help of ultrasound, it is possible to determine when the follicles will reach maturity.

Then, to stimulate ovulation, the woman is injected with another hormone, human chorionic gonadotropin. Human chorionic gonadotropin is produced during pregnancy and is similar to luteinizing hormone, which is normally released in the middle of the menstrual cycle. Alternatively, a gonadotropin-releasing hormone (GnRH) agonist can be used to induce ovulation, especially in women with a high risk of ovarian hyperstimulation syndrome. GnRH agonists are synthetic forms of a hormone (GnRH) that is produced by the body.

If human gonadotropins are used correctly, then more than 95% of women ovulate, but only about 50% of them become pregnant. In women who became pregnant after treatment with human gonadotropin, the incidence of multiple pregnancies ranges from 10 to 30% of cases, and these are mainly twins.

Human gonadotropins are expensive and can cause serious side effects, so doctors closely monitor the woman during treatment. Approximately 10-20% of women treated with human gonadotropin develop moderate or severe ovarian hyperstimulation syndrome.

Conclusions: thus: if a woman has a high risk of multiple pregnancies or the development of ovarian hyperstimulation syndrome, it is safer not to prescribe a drug to stimulate ovulation. But if it is necessary to induce ovulation, the use of a GnRH agonist is safer than the use of human chorionic gonadotropin. If the hypothalamus does not produce gonadotropin-releasing hormone, intravenous injections of a synthetic version of this hormone (gonadorelin acetate) can be used. This drug, like a natural hormone, stimulates the production of hormones by the pituitary gland that cause ovulation. With this treatment, the risk of ovarian hyperstimulation is extremely low, so careful monitoring is not required. However, this drug is not available in the United States of America.

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